

STUDIES IN AROMATIC NITRATION:
ADDITION-ELIMINATION MECHANISMS IN ELECTROPHILIC
AROMATIC SUBSTITUTION

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by

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A B S T R A C T

It has been found that the nitration of suitably substituted aromatic compounds in nitric acid-acetic anhydride at 0° gives a mixture of products, some of which result from attack by the nitrating species at substituted ring positions (ipso-nitration). From this and earlier work, it is now known that ipso-nitration may occur at ring positions substituted by either chloro, bromo, methyl, ethyl or methoxy groups. The product distributions suggest the factors determining the ratio of products arising from ipso-nitration and normal nitration are very sensitive to substituent changes. In general, however, provided the substituted ring position is of comparable reactivity to the available unsubstituted reaction sites, ipso-nitration is expected to be observed.

Among the products that may arise from ipso-nitration are nitrocyclohexadienones which rearrange to o-nitrophenols. The rearrangement mechanism of two of these dienones has been studied and found to be intermolecular, involving cleavage of the dienone into phenoxide and nitronium ions.

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I N T R O D U C T I O N

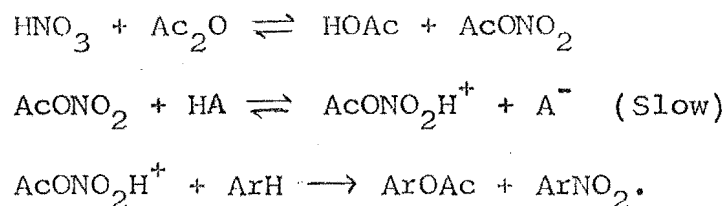
Nitric acid in acetic anhydride was first used as a nitrating agent by Orton¹ and the physical, and some chemical properties of this mixture were shown to be the same as those of an acetic acid solution of acetyl nitrate (prepared from acetic anhydride and nitrogen pentoxide^{2,2a}). However, although nitric acid-acetic anhydride mixtures have been used extensively in the preparation of aromatic nitro compounds, the nature of the actual nitrating agent and its mode of action remain doubtful. Nitration of a series of methylbenzenes in this medium was found to be accompanied by significant, sometimes major, amounts of acetoxylation to give aryl acetates³. Thus toluene and m-xylene gave small (< 5%) amounts of acetate while o-xylene produced 51% 3,4-dimethylphenyl acetate. These anomalous products were also found in the naphthalenes. For example, 1-methylnaphthalene gave an unspecified amount of an acetoxy derivative⁴.

Early studies of acetoxylation

Originally it was thought that the aryl acetates arose from electrophilic attack on the aromatic ring by protonated acetyl nitrate. This suggestion was based on kinetic studies of the nitration and acetoxylation of o-xylene and the product distributions obtained from the

methylbenzenes. An electrophilic acetoxylating species was indicated by the fact that the higher methylbenzenes generally gave greater yields of acetoxylation products. Sterically hindered positions were found to be poorly acetoxylated even though the highly acetoxylated unhindered positions were less active. o-Xylene, for example, with two ring positions almost equally activated for electrophilic attack, gave acetoxy products only in the unhindered 4-position, not in the 3-position which is flanked by a "buttressed" methyl group⁵. Similarly, in hemimellitene the 4-positions are more activated but also more hindered (by a "double-buttressed" methyl group) than the 5-position; the 5-position gave 35% acetoxy product and each 4-position only 5%. These observations were explained by postulating a bulky electrophile. The kinetic study⁶ showed that both the acetoxylation and nitration reactions for o-xylene were zeroth order in substrate concentration, that the addition of sulphuric acid or acetic acid to the reaction mixture accelerated both reactions and that in the presence of added lithium nitrate both were retarded. Most important, the ratio of the rates of acetoxylation and nitration remained constant under all reaction conditions over a very wide range of rates. This evidence suggested that nitration and acetoxylation occurred through a common species or a common precursor and the acceleration produced by sulphuric acid indicated a protonated species. Since

nitric acid in an excess of acetic anhydride was known to exist almost entirely as acetyl nitrate⁷ the obvious electrophile was protonated acetyl nitrate. If the rate-determining step was the formation of protonated acetyl nitrate, the reaction would be zeroth order in aromatic substrate as observed. The mechanism proposed as a result of these studies was that outlined in scheme I.



Scheme I

Evidence against electrophilic acetoxylation

This mechanism has subsequently been shown to be incorrect. It was based on the assumptions that the reaction was truly zeroth order in aromatic substrate and that acetates arose from electrophilic attack of an acetoxylating agent. These assumptions are now known to be invalid.

Studies on zeroth order kinetics in nitric acid-acetic anhydride mixtures

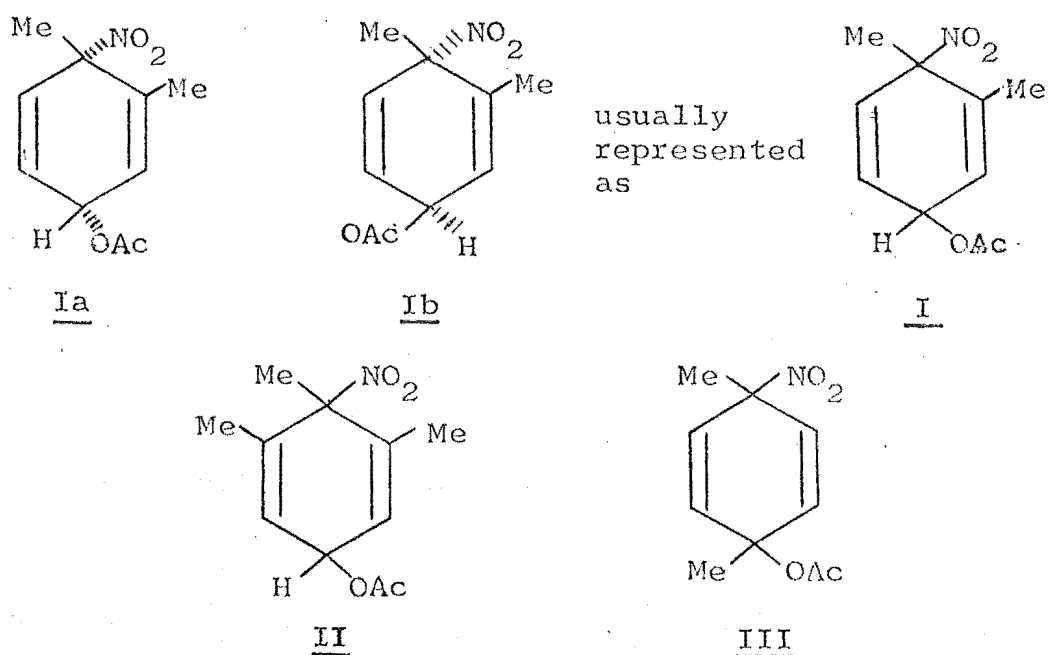
Recently doubts were raised⁸ concerning the authenticity of these apparently zeroth order reactions

involving nitric acid-acetic anhydride mixtures partly because the concentration of the aromatic compound required to attain the zeroth order was much greater in acetic anhydride than in other solvents. It was also found that the value of the "zeroth order" rate constant depended to some extent on the nature and concentration of the aromatic substrate. Thus for $[\text{ArH}] = \text{ca. } 0.5 \text{ mol.l}^{-1}$, the zeroth order rate with m-xylene was found to be 46% greater than that with o-xylene, and the zeroth order rate of nitration of anisole was increased by more than a factor of two when the substrate concentration increased from 0.1 to 1.0 mol.l^{-1} (9). Ridd et al.⁸ studied the nitration of benzene, toluene, m-xylene and mesitylene in acetic anhydride and established that the order with respect to the aromatic compound decreased from 1 to 0 as the concentration of aromatic compound increased. They interpreted this change in order as primarily a medium effect rather than rate-determining formation of the electrophile. The change in order with respect to aromatic substrate could be explained if high concentrations of aromatic compounds decreased the rate of nitration by a medium effect. The apparent zeroth-order reaction would then arise from the superposition of this medium effect on the normal first-order kinetic form; different substrates would then give different zeroth-order rates as observed.

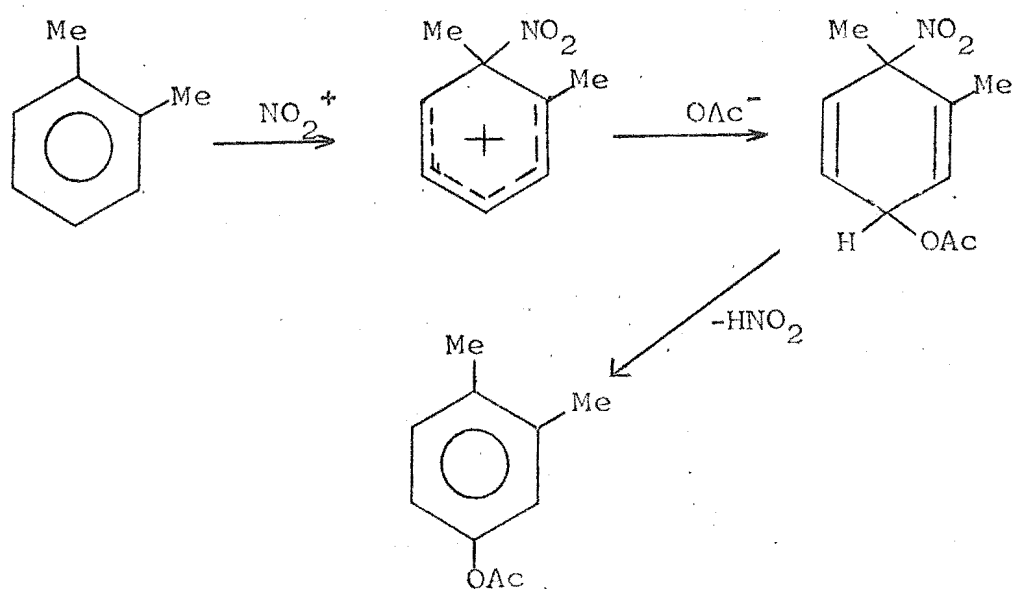
This hypothesis was tested by determining the effect of inert aromatic compounds (*p*-dichlorobenzene and 1,2,4-trichlorobenzene) on the rate of nitration of mesitylene. These two additives caused significant medium effects which were used as a model for the medium effects of the aromatic substrates studied; the corrected data for mesitylene and toluene nitration were found to adhere closely to first-order form even at high concentrations of aromatic compound (0.5 mol.l^{-1} mesitylene).

Evidence for an addition-elimination acetoxylation mechanism

A number of studies on nitration of di- and trimethylated benzene compounds in nitric acid-acetic anhydride by Blackstock resulted in the isolation of 1,4-acetoxy-nitro adducts which decomposed to aryl acetates in aqueous media. Thus *o*-xylene in nitric acid-acetic anhydride at 0° gave the cis and trans dienes (Ia, Ib) which decomposed to 4-acetoxy-*o*-xylene in aqueous media¹⁰. Hemimellitene gave diene (II) and *p*-xylene gave diene (III)¹¹ which, under the same decomposition conditions, gave ring-acetoxyated products. Diene (III), unlike the others, cannot rearomatise by simple nitrous acid loss and instead undergoes a 1-2 acetate shift to form 2-acetoxy-*p*-xylene.



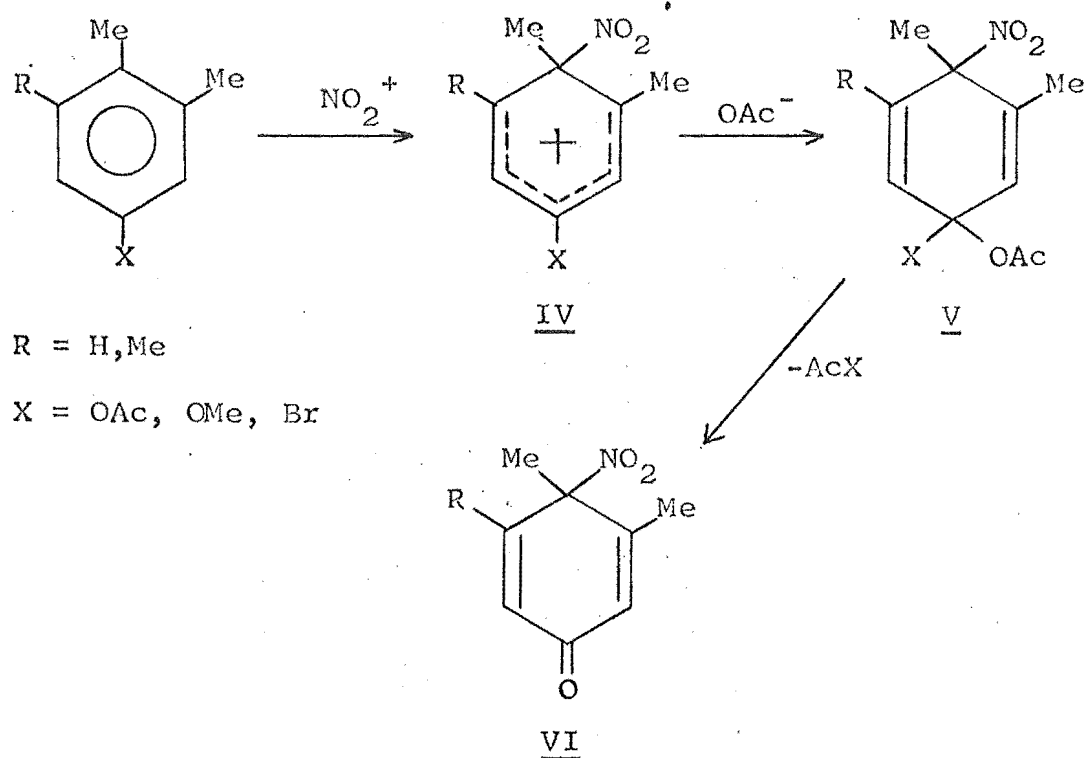
The isolation of such dienes and their quantitative decomposition to aryl acetates was proof that the acetate products observed in the nitration of *o*-xylene and hemimellitene were formed via the addition-elimination pathway (Scheme II) and not by electrophilic acetoxylation.



Scheme II

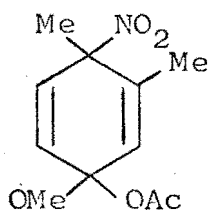
The initial attack by the nitrating species in nitric acid-acetic anhydride mixtures (represented here as NO_2^+) at a substituted ring position was termed ipso-nitration¹² and this term is now generally accepted in the literature.

Treatment of 5-substituted hemimellitenes and 4-substituted o-xylenes with nitric acid-acetic anhydride at 0° gave 4-nitro-cyclohexa-2,5-dien-1-ones as well as normal ring-substituted nitro products¹³. The suggested mechanism was similar to scheme II in that it consisted of ipso-attack at a methyl-substituted ring position followed by trapping of the resulting benzenonium ion (IV) by a nucleophile to give a diene (V).



Scheme III

Dienes of type (V) were not isolated at the time but were assumed to be very unstable and to rapidly eliminate AcX to give nitro-dienones (VI). It was found that reactions run at low temperatures (-50°) showed signals in the diene region of the n.m.r. spectrum. These peaks disappeared as the dienone signal appeared at the work-up temperature of 0° . This assumption was recently supported by the isolation of the cis and trans isomers of the adduct (VII) which decomposed readily to 3,4-dimethyl-4-nitro-cyclohexa-2,5-dien-1-one.⁹⁷ The dienones, in turn, rearranged in a number of solvents and gave nitrophenols as the major product.

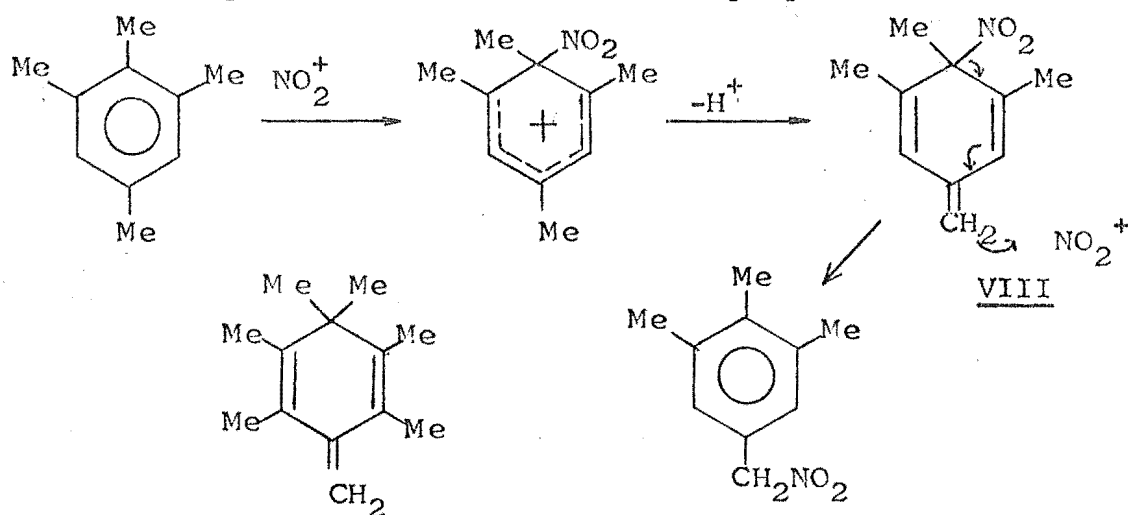


VII

The formation of side-chain nitro products

The addition-elimination mechanism was also used to explain the formation of side-chain nitro products isolated from the nitration of polymethylbenzenes by nitric acid-acetic anhydride at 0° ¹⁴. Pseudocumene, durene, isodurene, prehnitene and pentamethylbenzene all gave side-chain nitro products. In all these cases, the phenylnitromethane isomer formed was the one resulting from substitution on the methyl group para to the most activated methyl-substituted ring position; none of the hydrocarbons which did not have a methyl

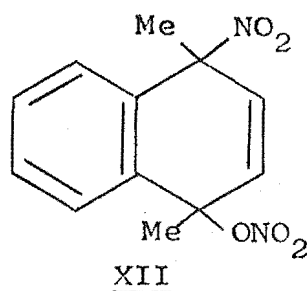
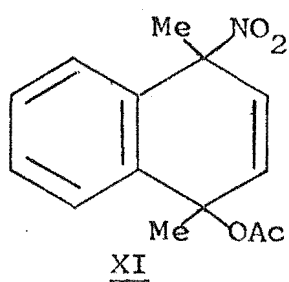
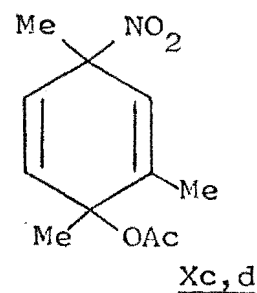
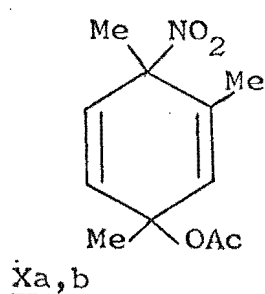
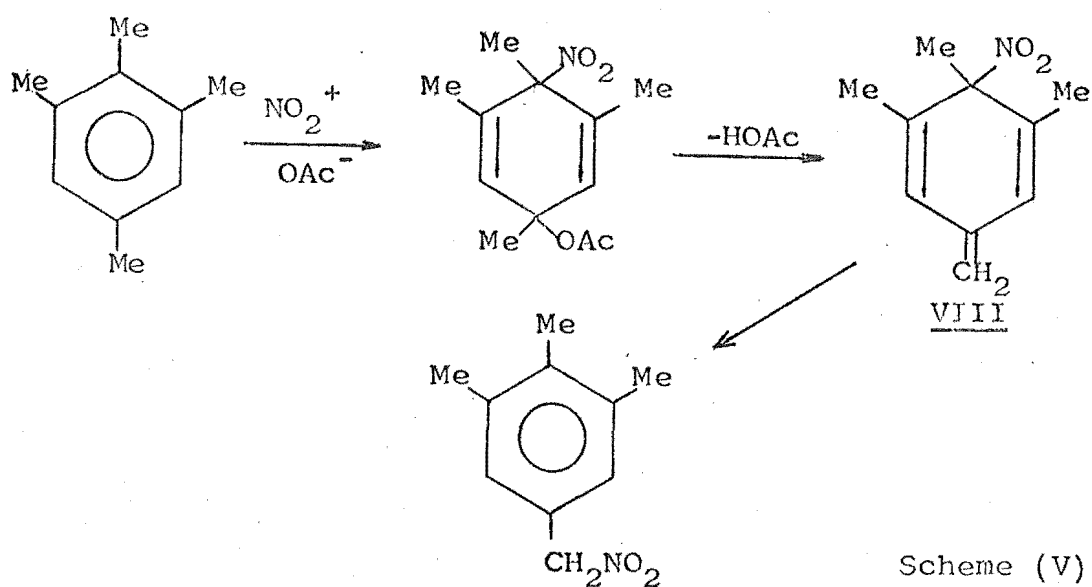
group para to such a position, e.g. mesitylene, gave side-chain products. The mechanism proposed was:-¹⁵



Scheme (IV)

The intermediate (IX), similar to (VIII) had been isolated from the methylation of hexamethylbenzene¹⁶ and results from the nitration of 1,4-dimethylnaphthalene^{17,17a} and chlorination of 1-methylnaphthalene by thionyl chloride¹⁸ supported such a mechanism.

A possible alternative mechanism leading to side-chain nitro products involved the formation of the methylenecyclohexadiene species (VIII) from the decomposition of a diene and not by proton loss from the benzenonium ion. (Scheme V). This was originally considered unlikely because a diene of this type isolated from the nitration of *p*-xylene (III) did not decompose in this manner. However, recently dienes (Xa-d) and (XI) were isolated^{19,20} and found to decompose to give side-chain nitro products. In the

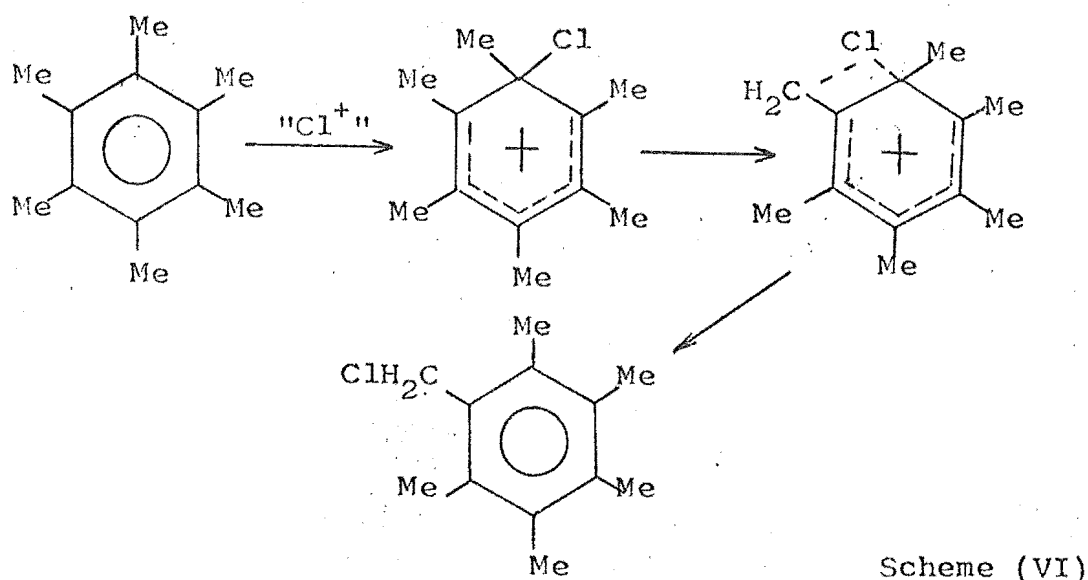


case of diene (XI) the decomposition was followed by n.m.r. but at no stage were there any major peaks observed which could be attributed to an exocyclic diene of type (VIII).²⁰ This suggested that if an exocyclic diene formed, it was more reactive than other intermediates in the reaction sequence. In spite of the lack of direct evidence for their

existence, the exocyclic dienes (VIII) are considered key intermediates in the formation of side-chain products for reasons explained in the discussion. During the course of one of the decomposition studies²⁰ evidence was obtained, at -60° , for the nitronium nitrate diene (XII). When the temperature was raised to -40° the signals of the diene (XI) appeared. This is the only case to date in which strong evidence for nitronium nitrate adducts has been reported although they have been postulated before²¹. It is clear that acetyl nitrate adducts (X,XI) are formed during the side-chain nitration of pseudocumene and 1,4-dimethylnaphthalene although they may not be necessary intermediates since they are in equilibrium with the initially formed nitronium nitrate adducts. It may be the nitronium nitrate adducts that are converted to the next step in the side-chain nitro formation. Doubt remains as to the exact mechanism by which side-chain nitro products arise from the nitration of polymethylbenzenes in nitric acid-acetic anhydride, but it is certain that the initial step is ipso-nitration at a methyl-substituted ring position.

Before Blackstock's nitration work on polymethylbenzenes, Bacchioci and Illuminati had chlorinated hexamethylbenzene using chlorine in anhydrous acetic acid and obtained a side-chain chloro product²².

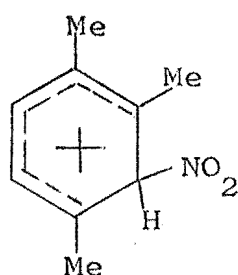
Their proposed mechanism was:-



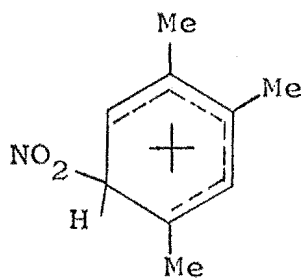
Side-chain halogenation also occurred in polymethylbenzenes with bromine²³ or ICl ²⁴ in acetic acid. Similar mechanisms had been proposed for these reactions.

However, scheme (VI) did not account for the products formed in Blackstock's nitration work. Scheme (VI), when applied to nitration, required the nitro group to rearrange from one methyl-substituted position to another methyl group ortho to it. In two cases, pseudocumene and isodurene, the side-chain nitration occurred on a methyl group which had only unsubstituted ring positions ortho to it. If side-chain nitration were to occur by an intramolecular transfer of the nitro group, it would mean that the rearrangement took place from the "normal" σ -complexes (XIII, XIV, XV). This was considered unlikely since such ions can readily rearomatise by proton loss and also because only one side-chain nitro product was

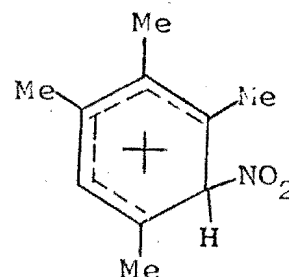
formed from each compound; (XIII) and (XV) could each transfer the nitro group to two different methyl groups.



XIII



XIV



XV

Addition products in other systems

Most of the earliest evidence for addition to aromatic systems was found in fused aromatic systems. In terms of resonance stabilisation energies it is not unexpected that such systems form adducts more easily than isolated rings. The stabilisation energy of naphthalene is 256 kJ/mole and the resonance energy of benzene is 152 kJ/mole²⁵. Thus the resonance energy lost by forming the acetoxychloride adduct isolated in the chlorination of naphthalene²⁶ is 104 kJ/mole. This figure does not allow for any conjugation from the double bond. The same applies to the formation of a tetrachloride and an acetoxychloride in the chlorination of 2-methylnaphthalene in acetic acid²⁷. Formation of the 9,10-addition product from anthracene²⁸ results in the loss of about 48 kJ/mole resonance stabilisation energy while in phenanthrene²⁹, 80 kJ/mole is lost. To form a diene

adduct from an isolated benzene ring system requires the loss of about 152 kJ/mole of resonance stabilisation. The instances where this occurs are correspondingly fewer although biphenyl is known to give a small amount of adduct³⁰ and certain methylated biphenyls give appreciable amounts of acetoxychloride adducts³¹.

As has been pointed out, these "anomalous" nitration products may not always be formed to indicate an addition-elimination mechanism³². If addition products are unstable under the conditions of reaction and especially if they decompose into the same products which are formed, or expected to be formed by direct electrophilic substitution, they will be very difficult to detect. Such a case occurs in the chlorination of phenanthrene where the dichloro adduct decomposes to give 9-chlorophenanthrene²⁹.

Scope of this thesis

The major features of the reaction of methylbenzenes with nitric acid-acetic anhydride are now clear. Ring nitro products are formed by normal electrophilic attack at an unsubstituted ring position and the key step in the formation of "anomalous" nitration products is ipso-nitration at a methyl-substituted ring position to form a benzenonium ion

which may add a nucleophile (usually acetate) to generate a pair of diastereoisomeric dienes. The dienes rearrange to give aryl acetates (scheme II) and possibly rearrange by loss of acetic acid to give the methylenecyclohexadiene (e.g. VIII); the intermediate in side-chain nitro formation.(scheme V). Alternatively, the methylenecyclohexadiene may arise directly by proton loss from the initial benzenonium ion.(scheme IV). When the diene is of type(V) it rearranges to give a dienone which in turn rearranges to a nitrophenol (scheme III).

This thesis examines three particular facets of the reaction of aromatic substrates in nitric acid-acetic anhydride mixtures: (i) the possibility of ipso-nitration at groups other than methyl, (ii) the sensitivity of ipso-nitration to substituent and steric effects and (iii) the mechanism by which the dienones rearrange to the nitrophenols.

EXPERIMENTAL

Melting points are uncorrected. N.m.r. spectra were run on a Varian A60 or Varian T60 machine in CCl_4 or CDCl_3 solution using TMS as an internal standard. Infrared spectra were run on a Shimadzu 227 spectrometer as smears, nujol mulls or KBr discs. Mass spectra were run on an AEI MS 902 mass spectrometer. Ultraviolet spectra were run in trifluoroethanol solvent on a Shimadzu MPS-50L spectrometer. Gas chromatography was carried out using a Varian Aerograph Model 1200 with a flame ionisation detector; peak areas were measured with a Kent Chromalog Integrator. Columns most often used were FFAP (3% on Chromosorb G), PDEAS (3% on Aeropak 30), PEGA ($2\frac{1}{2}\%$ on Aeropak 30), SE-30 (3% on Aeropak 30) and QF-1 (2% on Aeropak 30). Preparative gas chromatography was carried out on an Aerograph Autoprep Model 705.

Reagents

Nitric acid (s.g.1.52) was distilled from a mixture of concentrated sulphuric acid (2 volumes) and nitric acid (1 volume) at room temperature and 1 mm. pressure and stored in dry ice. Nitric acid prepared in this way contains less than 0.01 mole per cent nitrous acid and does not decompose significantly within several weeks at -64° ³³. Acetic anhydride (AR)

was refluxed over magnesium turnings for several days with silica gel drying tubes attached. It was fractionated on a 30-plate column; the fraction boiling between 139° and 140° was collected and used. Alumina for column chromatography was P. Spence, Grade H, deactivated by adding either 5% or 10% by weight of 10% aqueous acetic acid. Silica gel for column chromatography was Crosfield's "Sorbisil" Grade B.S.S. Solvents for column chromatography were technical grade. Light petroleum (50-70) was distilled off P_2O_5 and ether was distilled off sodium hydride and stored over sodium wire.

Preparation of aromatic substrates

para-Diethylbenzene was prepared by acylation of ethylbenzene³⁴ and reduction of this ketone with Zn/Hg amalgam³⁵. It had b.p. $183^{\circ}/760$ mm. (lit. $183^{\circ}/760$ mm.³⁶).

para-Ethyltoluene was prepared by acylation of toluene³⁷ and reduction of the resulting ketone by Zn/Hg amalgam³⁵. It had b.p. $162^{\circ}/760$ mm. (lit. $161-2^{\circ}/760$ mm.³⁶).

Ethylmesitylene was prepared by acylation of mesitylene³⁸ and reduction of the resulting ketone with Zn/Hg amalgam³⁵. It had b.p. $212-5^{\circ}/760$ mm. (lit. $210^{\circ}/725$ mm.³⁹).

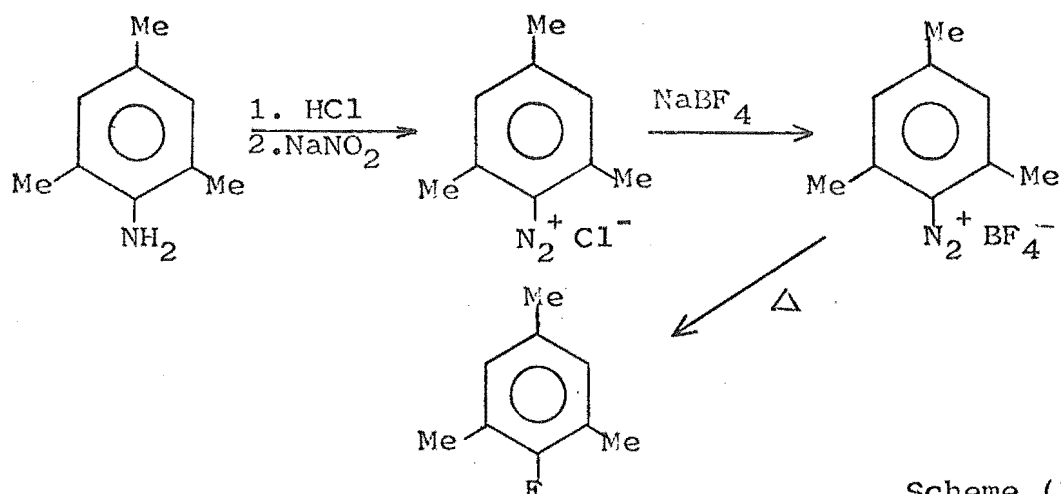
Bromomesitylene was prepared by bromination of mesitylene⁴⁰. It had b.p. $222^{\circ}/760$ mm. (lit. $105-7^{\circ}/17$ mm⁴⁰).

2,4,6-Trimethoxybromobenzene was prepared by the methylation of phloroglucinol^{41, 41a} and bromination of the resulting phloroglucinol trimethylether⁴². It had m.p. $96-7^{\circ}$ (lit. $97-9^{\circ}$ ⁴²).

Chloromesitylene was prepared by the chlorination of mesitylene⁴³. It had b.p. $206-7^{\circ}/760$ mm. (lit. $204-6^{\circ}/760$ mm.⁴³).

2,4,6-Trimethoxychlorobenzene was prepared by the chlorination of phloroglucinol trimethylether with sulphuryl chloride⁴⁴ and by the chlorination of phloroglucinol trimethylether with phosphorus pentachloride⁴⁵. It had m.p. $92-3^{\circ}$ (lit. 93° ⁴⁵).

Fluoromesitylene was prepared from mesidine by the following method (Scheme VII).

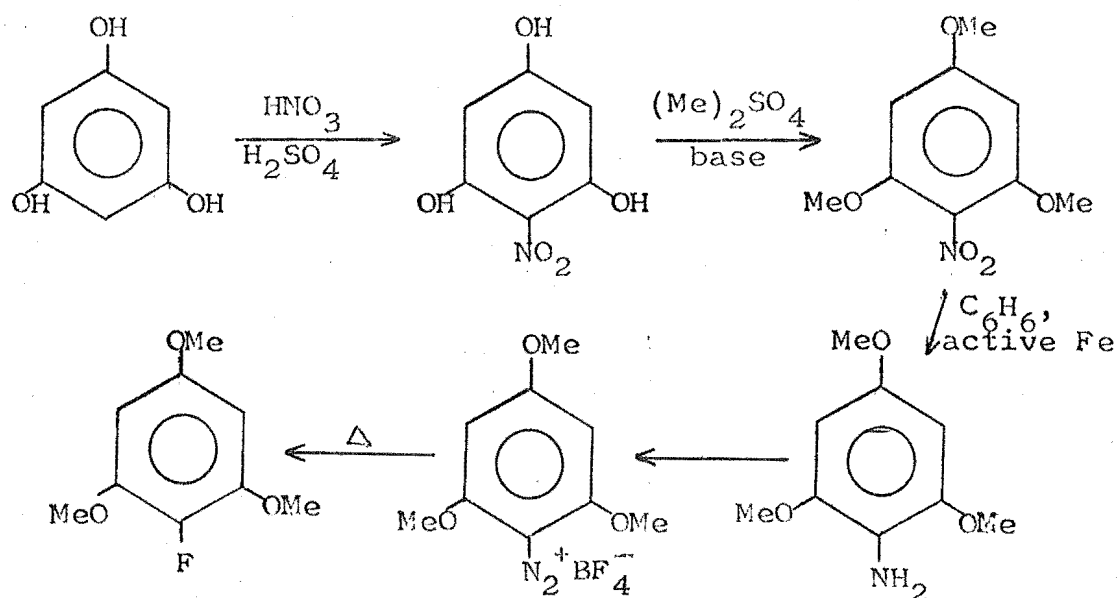


Scheme (VII)

The diazonium tetrafluoroborate was prepared from mesidine by diazotisation with nitrous acid and hydrochloric acid, followed by the addition of a cold, aqueous solution of sodium tetrafluoroborate. The resulting precipitate was dried and decomposed to give fluoro-

mesitylene⁴⁶. It had b.p. 167°/760 mm. (lit. 168.5-168.7/760 mm.⁴³).

2,4,6-Trimethoxyfluorobenzene was prepared from phloroglucinol by the following method (Scheme VIII).



Scheme (VIII)

Mononitrophloroglucinol was prepared by the nitration of phloroglucinol⁴⁷ and methylated⁴¹ to give mononitrophloroglucinol trimethylether. This was reduced to the corresponding amine by treatment with active iron and benzene^{48,49}. 2,4,6-Trimethoxyfluorobenzene was prepared from the amine as a thick colourless oil by the method used in Scheme VII.

Methoxymesitylene was prepared from freshly distilled mesidine by diazotisation and hydroxylation⁵⁰ and methylation of the resulting mesitol⁴¹. It had b.p. 200°/760 mm. (lit. b.p. 29°/0.4-0.45 mm.⁵¹).

2,4,6-Trimethylbiphenyl was prepared from aniline

and mesitylene by the Gomberg-Bachmann-Hey method ⁵². It was washed with hydroferrichloric acid ⁵³ and obtained as a yellow liquid; b.p. 275°/760 mm. (lit. 275-7/760mm. ⁵²).

2,2',4,4',6,6'-hexamethoxybiphenyl was prepared from phloroglucinol trimethylether and benzene by the method of Norman et al. ⁵⁴. It was hoped that the product of this reaction would be 2,4,6-trimethoxybiphenyl but in fact it gave a 50:50 mixture of biphenyl and hexamethoxybiphenyl which was separated by column chromatography. 2,4,6-trimethoxybiphenyl could not be made by any of the conventional methods.

4-Methoxybiphenyl was prepared from anisidine and benzene by the Gomberg-Bachmann-Hey method ⁵². It had m.p. 89-90° (lit. 88-9° ⁵⁵).

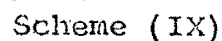
4-Bromobiphenyl was a commercial sample recrystallised from ethanol to give white crystals; m.p. 89° (lit. 89.5-90° ⁵⁶).

para-Methoxytoluene was prepared by the methylation of para-cresol ⁵⁷. It had b.p. 174-6°/760 mm. (lit. 174/758 mm. ⁵⁸).

para-Bromotoluene was a commercial sample purified by column chromatography and recrystallisation from light petroleum: ether.

para-Acetoxytoluene and acetoxyprehnitene were prepared by the acetoxylation of the appropriate phenols ⁵⁹.

5-Fluorohemimellitene was prepared by the following method (Scheme IX). Isophorone oxime was prepared by



the reaction of isophorone and hydroxylamine in pyridine and methanol. The oxime was treated with acetyl chloride in acetic anhydride and pyridine to form a mixture of 3,4,5-trimethylacetanilide and 2,4,5-trimethylacetanilide. The mixed acetanilides were refluxed with 20% sulphuric acid to give the corresponding anilines. After distillation and recrystallisation from pentane, the 5-aminoheptamellitene was obtained pure ⁶⁰ and converted to the diazonium tetrafluoroborate salt, a white solid decomposing at

85-6° to give 5-fluorohemimellitene as a colourless liquid; b.p. 182-3°/760 mm.

5-Bromopseudocumene was prepared by the bromination of pseudocumene⁶¹. It had m.p. 70° (lit. 71°⁶¹).

3,4,5-Trimethylacetanilide was prepared from the amine made as precursor to 5-fluorohemimellitene; recrystallisation of the crude product from ether gave yellow crystals; m.p. 166° (lit. 166°⁶²).

ortho-Xylene was a commercial sample purified by distillation through a 30 cm. Vigreux column to give greater than 98% pure o-xylene (g.l.c.).

para-Bromoethylbenzene was a commercial sample purified by distillation through a 60 cm. Nester-Faust annular teflon spinning band.

All starting materials were greater than 98% pure by g.l.c.

General Nitration Procedure

For analytical runs, the aromatic compound (0.5g) was dissolved in acetic anhydride (2 ml.) and cooled to 0°. Nitric acid (0.1 ml.) dissolved in acetic anhydride (1 ml.) was run in dropwise with stirring. After 1½ hours the reaction mixture was quenched in water (50 ml.), extracted with ether (20-30 ml.), the ether extract washed with water and dried over magnesium sulphate. After removal of the ether the sample was analysed by g.l.c. An estimate of the amount of dienes and

dienones present was obtained from the n.m.r. spectrum of the crude reaction mixture. This was always in close agreement with the amount of diene and dienone decomposition products indicated by g.l.c. analysis.

For preparative runs more nitric acid was used, usually in the ratio of 2 moles nitric acid to 1 mole of aromatic compound. The work-up procedure used was one or both of the following:-

(1) After nitrating as above, the reaction mixture was pumped under vacuum at or below room temperature to remove solvent. This was a lengthy procedure (1-2 days) and the result was in nearly every case a yellow oil which was adsorbed onto alumina or silica for column chromatography.

(2) After nitrating as above, the reaction mixture was quenched in CCl_4 (200 ml. for 5 g. aromatic substrate). The CCl_4 was washed with water and dried with magnesium sulphate and the CCl_4 removed under vacuum at room temperature. The resulting yellow oil was chromatographed as described below.

Isolation of final products

para-Diethylbenzene (8 g.) was nitrated and worked up by both methods. In both cases the residue was adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 2-nitro-1,4-diethylbenzene as a yellow liquid, b.p. $254-8^\circ/760$ (lit. $137-40/12^{63}$);

n.m.r. (CCl_4) $\delta = 1.25$ (t, $J = 8$ c.p.s. ArCH_2CH_3 , 6H), 2.71 (q, $J = 8$ c.p.s. ArCH_2CH_3 , 2H), 2.89 (q, $J = 8$ c.p.s. ArCH_2CH_3 , 2H), 7.30 (s, ArH , 2H), 7.75 (s, ArH , 1H); I.R. (smear) 1530, 1330, 1055, 790 cm^{-1} ; mass spectrum, m/e 179 (M^+) (Found m/e 179.094495. Calc. for $\text{C}_{10}\text{H}_{13}\text{NO}_2$: 179.094263). Elution with 49:1 light petroleum:ether gave 4-(α -nitroethyl)-ethylbenzene as white crystals; m.p. 75° ; n.m.r. (CCl_4) $\delta = 1.30$ (t, $J=8$ c.p.s. ArCH_2CH_3 , 3H), 1.65 (d, $J=8$ c.p.s. $\text{ArCHNO}_2\text{CH}_3$, 3H), 2.75 (q, $J=8$ c.p.s. ArCH_2CH_3 , 2H), 6.00 (q, $J = 8$ c.p.s. $\text{ArCHNO}_2\text{CH}_3$, 1H), 7.39 (broad s, ArH , 4H); I.R. (KBr) 1530, 1355, 850 cm^{-1} ; mass spectrum, m/e 179 (M^+) (Found m/e 179.094461. $\text{C}_{10}\text{H}_{13}\text{NO}_2$ requires mol. wt. 179.094263). Elution with 32:1 light petroleum:ether brought through 2-acetoxy-1,4-diethylbenzene as a colourless liquid; b.p. $233-9^\circ/760$; n.m.r. (CCl_4) $\delta = 1.30$ (t, $J = 8$ c.p.s. ArCH_2CH_3 , 6H), 2.02 (s, ArOAc , 3H), 2.76 (q, $J = 8$ c.p.s. ArCH_2CH_3 , 2H), 2.88 (q, $J = 8$ c.p.s. ArCH_2CH_3 , 2H), 7.35 (s, ArH , 2H), 7.85 (s, ArH , 1H); I.R. (smear) 1730, 1225, 865 cm^{-1} ; mass spectrum, m/e 192 (M^+) (Found m/e 192.115543. $\text{C}_{12}\text{H}_{16}\text{O}_2$ requires mol. wt. 192.115023). Further elution with 32:1 light petroleum:ether gave one of the isomers of 1,4-diethyl-1-acetoxy-4-nitro-cyclohexa-2,5-diene as a yellow oil; n.m.r. (CCl_4) $\delta = 1.25$ (t, $J=8$ c.p.s. ArCH_2CH_3 , 6H), 2.00 (s, ArOAc , 3H), 2.72 (q, $J=8$ c.p.s. ArCH_2CH_3 , 2H), 2.90 (q, $J=8$ c.p.s. ArCH_2CH_3 , 2H), 6.10 (s, diene protons, 4H); I.R. (smear)

1740, 1540, 1370, 1220 cm^{-1} ; u.v. (TFE) $\lambda_{\text{max}} = 197.5 \text{ nm}$, $\epsilon = 16,300$. The diene isomer decomposed into more than one product. A sample of the isomer was heated in acetic acid containing a little nitromethane as a standard, and the proportions of the products formed determined by n.m.r. analysis of the mixture after heating. The decomposition products were p-diethylbenzene and 2-acetoxy-1,4-diethylbenzene in the ratio 1:2. Before work-up of the nitration mixture there was n.m.r. evidence of the other diene isomer but it was much more reactive and was not isolated.

para-Ethyltoluene (10 g) was nitrated, worked up by method (2) and adsorbed onto 10% deactivated alumina. Elution with light petroleum gave a mixture of 2- and 3-nitro-4-ethyltoluene. These were separated by further chromatography on 10% deactivated alumina to give 3-nitro-4-ethyltoluene as a clear liquid; b.p. 255/760 (lit. 115-20/10⁶⁴); n.m.r. (CCl_4) $\delta = 1.20$ (t, $J=8$ c.p.s. ArCH_2CH_3 , 3H), 2.43 (s, ArCH_3 , 3H), 2.85 (q, $J=8$ c.p.s. ArCH_2CH_3 , 2H), 7.25 (s, ArH , 2H), 7.70 (s, ArH , 1H); I.R. (smear) 1535, 1335, 860 cm^{-1} ; mass spectrum, m/e 165 (M^+) (Found m/e 165.078102. Calc. for $\text{C}_9\text{H}_{11}\text{NO}_2$ 165.078973). This compound was reduced to the corresponding amine; b.p. 235^o/760 (lit. 110^o/10⁶⁴), acetanilide; m.p. 142^o (lit. 142^o 64). 2-Nitro-4-ethyltoluene was obtained as a clear liquid; b.p. 248^o/760 (lit. 248^o 65); n.m.r. (CCl_4) $\delta = 1.20$ (t, $J=8$ c.p.s.

ArCH_2CH_3 , 3H), 2.64 (s, ArCH_3 , 3H), 2.69 (q, J=8 c.p.s. ArCH_2CH_3 , 2H), 7.25 (s, ArH , 2H), 7.70 (s, ArH , 1H); I.R. (smear) 1535, 1335, 855 cm^{-1} ; mass spectrum, m/e 165 (M^+) (Found m/e 165.078396. Calc. for $\text{C}_9\text{H}_{11}\text{NO}_2$ 165.078973). This compound was reduced to the corresponding amine; b.p. $231^\circ/760$ (lit. $220-230^\circ/773^{65}$), acetanilide; m.p. 135° (lit. 136°^{65}). Elution with 49:1 light petroleum:ether gave 4-ethyl-phenylnitromethane as a liquid; b.p. $115-18^\circ/760$; n.m.r. (CCl_4) $\delta = 1.27$ (t, J=8 c.p.s. ArCH_2CH_3 , 3H), 2.66 (q, J=8 c.p.s. ArCH_2CH_3 , 2H), 5.32 (s, ArCH_2NO_2 , 2H), 7.27 (s, ArH , 4H); I.R. (smear) 1530, 1325, 830 cm^{-1} ; mass spectrum m/e 165 (M^+) (Found m/e 165.078962. $\text{C}_9\text{H}_{11}\text{NO}_2$ requires mol. wt. 165.078973). Further elution with 49:1 light petroleum:ether gave 4-(α -nitroethyl)-toluene as a pale yellow liquid; b.p. $80-1^\circ/760$; n.m.r. (CCl_4) $\delta = 1.62$ (d, J=8 c.p.s. $\text{ArCHNO}_2\text{CH}_3$, 3H), 2.60 (s, ArCH_3 , 3H), 5.92 (q, J=8 c.p.s. $\text{ArCHNO}_2\text{CH}_3$, 1H), 7.44 (broad s, ArH , 4H); I.R. (smear) 1535, 1330, 855 cm^{-1} ; mass spectrum, m/e 165 (M^+) (Found m/e 165.078812. $\text{C}_9\text{H}_{11}\text{NO}_2$ requires mol. wt. 165.078973). Elution with 32:1 light petroleum:ether gave 2-acetoxy-4-(α -nitroethyl)-toluene as a yellow oil; n.m.r. (CCl_4) $\delta = 1.53$ (d, J=8 c.p.s. $\text{ArCHNO}_2\text{CH}_3$, 3H), 2.05 (s, ArOAc , 3H), 2.59 (s, ArCH_3 , 3H), 5.85 (q, J=8 c.p.s. $\text{ArCHNO}_2\text{CH}_3$, 1H), 7.35 (s, ArH , 2H), 7.85 (s, ArH , 2H); I.R. (smear) 1745, 1535, 1330, 1225 cm^{-1} ; mass spectrum m/e 223 (M^+) (Found m/e 223.084374. $\text{C}_{11}\text{H}_{13}\text{NO}_4$ requires

mol. wt. 223.084451). This compound was oxidised by the method of Schecter and Williams⁶⁶ and the resulting product hydrolysed by boiling in hydrochloric acid to give 3-hydroxy-4-methyl-acetophenone; m.p. 110° (lit. 111°⁶⁷). This established the initial product as 2-acetoxy-4-(α -nitroethyl)-toluene since 2-hydroxy-4-methyl-acetophenone is a liquid; b.p. 91-3°/5⁶⁸. Elution with 21:1 light petroleum:ether gave 3-acetoxy-4-ethyltoluene as a pale yellow liquid; n.m.r. (CCl₄) δ = 1.25 (t, J=8 c.p.s. ArCH₂CH₃, 3H), 2.02 (s, ArOAc, 3H), 2.56 (s, ArCH₃, 3H), 2.81 (q, J=8 c.p.s. ArCH₂CH₃, 2H), 7.35 (s, ArH, 2H), 7.86 (s, ArH, 1H); I.R. (smear) 1735, 1225, 860 cm⁻¹; mass spectrum, m/e 178 (M⁺) (Found m/e 178.099226. Calc. for C₁₁H₁₄O₂ 178.099373). This product was established as the 3-isomer by treatment with concentrated sulphuric acid to give 6-ethyl-m-cresol as white crystals; m.p. 41-2° (lit. 42-4°⁶⁹). 4-Ethyl-o-cresol is a liquid; b.p. 224°/760⁷⁰.

Ethylmesitylene (5 g.) was nitrated and worked up by method (2). As CCl₄ was evaporated, white crystals formed. These were filtered and recrystallised from ether to give 3,5-dimethyl-4-ethyl-phenylnitromethane; m.p. 88-9°; n.m.r. (CCl₄) δ = 1.15 (t, J=7.5 c.p.s. ArCH₂CH₃, 3H), 2.35 (s, ArCH₃, 6H), 2.76 (q, J=7.5 c.p.s. ArCH₂CH₃, 2H), 5.40 (s, ArCH₂NO₂, 2H), 7.19 (s, ArH, 2H); I.R. (KBr) 1540, 1345, 850 cm⁻¹; mass spectrum, m/e 193 (M⁺) (Found m/e 193.110961. C₁₁H₁₅NO₂ requires mol. wt. 193.110272). A small amount of nitroethyl-

mesitylene, identical to an authentic sample, was isolated by column chromatography on 10% deactivated alumina.

Bromomesitylene (5 g.) was nitrated, worked up with CCl_4 and adsorbed on to 10% deactivated alumina.

Elution with light petroleum gave 2,4-dibromo-6-nitro-mesitylene as white crystals; m.p. $162-3^\circ$; n.m.r.

(CCl_4) $\delta = 2.32$ (s, ArCH_3 , 6H), 2.70 (s, ArCH_3 , 3H); I.R.

(KBr) $1535, 1350, 845 \text{ cm}^{-1}$; mass spectrum, m/e 325 (M^+)

(Found m/e 322.898217. $\text{C}_9\text{H}_9\text{NO}_2\text{Br}^{79}\text{Br}^{81}$ requires mol. wt.

322.898134). Elution with 20:1 light petroleum:ether

gave nitro-bromomesitylene as white crystals; m.p.

56° (lit. $54-6^\circ$ ⁷¹); n.m.r. (CCl_4) $\delta = 2.20$ (s, ArCH_3 , 3H),

2.35 (s, ArCH_3 , 3H), 2.42 (s, ArCH_3 , 3H), 7.00 (s, ArH , 1H);

I.R. (KBr) $1530, 1345, 840 \text{ cm}^{-1}$; mass spectrum m/e

243 (M^+) (Found m/e 242.989481. Calc. for $\text{C}_9\text{H}_{10}\text{NO}_2\text{Br}^{79}$

242.989539). Elution with 17:1 light petroleum:ether

gave nitromesitylene m.p. 44° (lit. 44° ⁷²) identical

with an authentic sample.

2,4,6-Trimethoxybromobenzene was nitrated, worked up with CCl_4 and adsorbed onto silica gel. Elution

with 4:1 light petroleum:ether gave a mixture of

1,3,5-tribromo-2,4,6-trimethoxybenzene and 1,3-dibromo-5-nitro-2,4,6-trimethoxybenzene. Attempts to separate

these compounds by further chromatography and g.l.c.

were not completely successful. The tri-bromo compound

(85-90% pure) had n.m.r. (CDCl_3) $\delta = 3.92$ (s, ArOCH_3);

I.R. (nujol) 1080, 925 cm^{-1} ; mass spectrum m/e 408 (M^+) (Found m/e 403.809263. $\text{C}_9\text{H}_9\text{O}_3\text{Br}_2$ ^{79}Br ^{81}Br requires mol. wt. 403.808364). 1,3-Dibromo-5-nitro-2,4,6-trimethoxybenzene (80%) had n.m.r. (CDCl_3) δ = 3.88 (s, ArPCH_3 , 3H), 3.95 (s, ArOCH_3 , 6H); I.R. (nujol) 1535, 1355, 920 cm^{-1} ; mass spectrum, m/e 373 (M^+) (Found m/e 370.883594. $\text{C}_9\text{H}_9\text{NO}_5\text{Br}^{79}\text{Br}^{81}$ requires mol. wt. 370.882876). Elution with 1:1 light petroleum:ether gave nitro-2,4,6-trimethoxybromobenzene as white crystals; m.p. $141-2^\circ$; n.m.r. (CDCl_3) δ = 3.89 (s, ArOCH_3 , 3H), 3.97 (s, ArOCH_3 , 6H), 6.34 (s, ArH , 1H); I.R. (KBr) 1540, 1345, 1110, 905, 800 cm^{-1} ; mass spectrum m/e 293 (M^+) (Found m/e 290.975316. $\text{C}_9\text{H}_{10}\text{NO}_5\text{Br}^{79}$ requires mol. wt. 290.974281). Elution with 3:2 ether:light petroleum gave 2,4,6-trimethoxynitrobenzene as white crystals; m.p. 152° (lit. $151-2^\circ$ ⁷³); n.m.r. (CDCl_3) δ = 3.78 (s, ArOCH_3 , 3H), 3.85 (s, ArOCH_3 , 6H), 6.35 (s, ArH , 2H); I.R. (KBr) 1540, 1360, 1110 cm^{-1} ; mass spectrum, m/e 213 (M^+) (Found m/e 213.063124. Calc. for $\text{C}_9\text{H}_{11}\text{NO}_5$ 213.063716).

Chloromesitylene (5 g.) was nitrated, worked up in CCl_4 and the residue adsorbed onto 10% deactivated alumina and eluted with light petroleum to give nitrochloromesitylene as white crystals; m.p. 56° (lit. $56-7^\circ$ ⁷⁴); n.m.r. (CCl_4) δ = 2.27 (s, ArCH_3 , 3H), 2.35 (s, ArCH_3 , 3H), 2.42 (s, ArCH_3 , 3H), 7.03 (s, ArH , 1H); I.R. (KBr) 1525, 1350, 850 cm^{-1} ; mass spectrum, m/e 199 (M^+) (Found m/e 199.039559. Calc. for $\text{C}_9\text{H}_{10}\text{NO}_2\text{Cl}^{35}$ 199.040002).

Elution with 6:1 light petroleum:ether gave dinitro-chloromesitylene as white crystals; m.p. $175-6^{\circ}$ (lit. 177° ⁷⁵); n.m.r. (CCl_4) $\delta = 2.35$ (s, ArCH_3 , 3H), 2.44 (s, ArCH_3 , 6H); I.R. (KBr) 1530, 1340, 870 cm^{-1} ; mass spectrum, m/e 244 (M^+) (Found m/e 244.025682. Calc. for $\text{C}_9\text{H}_9\text{N}_2\text{O}_4\text{Cl}^{35}$ 244.025079). Elution with 5:1 light petroleum:ether gave 3,5-dimethyl-4-chloro-phenylnitromethane as a white solid. Recrystallisation from ether:pentane (1:1) gave white crystals; m.p. $63-4^{\circ}$; n.m.r. (CDCl_3) $\delta = 2.40$ (s, ArCH_3 , 6H), 5.25 (s, ArCH_2NO_2 , 2H), 7.15 (s, ArH , 2H); I.R. (KBr) 1540, 1355, $1050, 855\text{ cm}^{-1}$; mass spectrum m/e 199 (M^+) (Found m/e 199.040215. $\text{C}_9\text{H}_{10}\text{NO}_2\text{Cl}^{35}$ requires mol. wt. 199.040002).

2,4,6-Trimethoxychlorobenzene (5 g.) was nitrated and worked up by both methods to give an oil in each case. This was adsorbed onto silica gel and eluted with 20:1 light petroleum:ether to give 3-nitro-2,4,6-trimethoxychlorobenzene as white crystals; m.p. 64° ; n.m.r. (CDCl_3) $\delta = 3.90$ (s, ArOCH_3 , 3H), 3.97 (s, ArOCH_3 , 6H), 6.39 (s, ArH , 1H); I.R. (KBr) 1540, 1340, 930 cm^{-1} ; mass spectrum, m/e 247 (M^+) (Found m/e 247.032174. $\text{C}_9\text{H}_9\text{NO}_5\text{Cl}^{35}$ requires mol. wt. 247.032569). Elution with 5:2 light petroleum:ether brought through 3,5-dimethoxy-4-chloro-4-nitro-cyclohexa-2,5-dien-1-one as a yellow oil; n.m.r. (CDCl_3) $\delta = 3.82$ (s, ArOCH_3 , 6H), 5.65 (s, diene protons, 2H); I.R. (smear) 1670, 1605, 1540, 1365, 910 cm^{-1} ; mass spectrum, m/e 233 (M^+) (Found m/e 233.009054. $\text{C}_8\text{H}_8\text{NO}_5\text{Cl}^{35}$

requires mol. wt. 233.009095); ultraviolet (TFE) λ 199.5nm. ϵ 11600. This compound decomposed to 4-chloro-3,5-dimethoxy-2-nitrophenol on standing at room temperature for ten days. The phenol had m.p. $91-2^\circ$; n.m.r. (CCl_4) δ = 3.97 (s, ArOCH_3 , 3H), 4.06 (s, ArOCH_3 , 3H), 6.47 (s, ArH , 1H), 9.83 (s, ArOH , 1H); I.R. (KBr) 3300, 1535, 1330cm^{-1} ; mass spectrum, m/e 233 (M^+) (Found m/e 233.009216. $\text{C}_8\text{H}_8\text{NO}_5\text{Cl}^{35}$ requires mol. wt. 233.009095).

Fluoromesitylene (3g.) was nitrated and worked up in CCl_4 . The residue was adsorbed onto 10% deactivated alumina. Elution with light petroleum gave nitrofluoromesitylene as white crystals; m.p. 43° (lit. $43-4^\circ$ ⁷⁶); n.m.r. (CCl_4) δ = 2.22 (s, ArCH_3 , 3H), 2.23 (s, ArCH_3 , 3H), 2.27 (s, ArCH_3 , 3H), 6.95 (d, $J=8$ c.p.s., ArH , 1H); I.R. (KBr) 1530, 1345, 800cm^{-1} ; mass spectrum, m/e 183 (M^+) (Found m/e 183.069114. Calc. for $\text{C}_9\text{H}_{10}\text{NO}_2\text{F}$ 183.069551). Elution with 35:1 light petroleum:ether gave dinitrofluoromesitylene as white crystals; m.p. 95° (lit. $95-96.5^\circ$ ⁷⁶); n.m.r. (CCl_4) δ = 2.10 (s, ArCH_3 , 3H), 2.15 (s, ArCH_3 , 6H); I.R. (KBr) 1535, 1350, 805cm^{-1} ; mass spectrum, m/e 228 (M^+) (Found m/e 228.053979. Calc. for $\text{C}_9\text{H}_9\text{N}_2\text{O}_4\text{F}$ 228.054628).

2,4,6-Trimethoxyfluorobenzene (1g.) was nitrated and worked up by the CCl_4 method. The residue was adsorbed onto silica gel. Elution with light petroleum gave nitro-2,4,6-trimethoxyfluorobenzene as white crystals; m.p. 61° ; n.m.r. (CCl_4) δ = 3.94 (s, ArOCH_3 , 3H), 4.02 (s, ArOCH_3 , 6H), 6.36 (d, $J=8$ c.p.s., ArH , 1H); I.R. (KBr)

1540, 1355, 805 cm^{-1} ; mass spectrum, m/e 231 (M^+) (Found m/e 231.053876. $\text{C}_9\text{H}_{10}\text{NO}_5\text{F}$ requires mol. wt. 231.054293). The remainder of the product mixture ($<5\%$) was an intractable gum.

Methoxymesitylene (3g.) was nitrated and worked up in CCl_4 . The oil was adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 2,4,6-trimethyl-4-nitrocyclohexa-2,5-dien-1-one as a yellow oil; n.m.r. (CCl_4) δ = 1.83 (s, ArCH_3 , 3H), 1.97 (s, ArCH_3 , 6H), 6.83 (s, diene protons, 2H); I.R. (smear) 1680, 1650, 1615, 1550, 1355 cm^{-1} ; mass spectrum, m/e 181 (M^+) (Found m/e 181.073523. $\text{C}_9\text{H}_{11}\text{NO}_3$ requires mol. wt. 181.073887); ultraviolet (TFE) λ 197nm. ϵ 14,200. This compound decomposed on heating to 150° in the gas chromatograph to give mesitol but was stable for several months at 0° . Elution with 32:1 light petroleum: ether gave 3,5-dimethyl-4-methoxyphenylnitromethane as a pale yellow oil; n.m.r. (CCl_4) δ = 2.17 (s, ArCH_3 , 6H), 3.71 (s, ArOCH_3 , 3H), 5.40 (s, ArCH_2NO_2 , 2H), 7.23 (s, ArH , 2H); I.R. (smear) 1535, 1345, 1110, 910 cm^{-1} ; mass spectrum, m/e 195 (M^+) (Found m/e 195.090110. $\text{C}_{10}\text{H}_{13}\text{NO}_3$ requires mol. wt. 195.089537). Elution with 21:1 light petroleum: ether brought through 2-acetoxy-3,5-dimethyl-4-methoxyphenylnitromethane as a yellow oil; n.m.r. (CDCl_3) δ = 2.03 (s, ArOAc , 3H), 2.27 (s, ArCH_3 , 3H), 2.32 (s, ArCH_3 , 3H), 3.78 (s, ArOCH_3 , 3H), 5.23 (s, ArCH_2NO_2 , 2H), 7.13 (s, ArH , 1H); I.R. (smear) 1745, 1530, 1340, 1220,

1050 cm^{-1} ; mass spectrum, m/e 253 (M^+) (Found m/e 253.096028. $\text{C}_{12}\text{H}_{15}\text{NO}_5$ requires mol. wt. 253.095014).

2,4,6-Trimethylbiphenyl (5g.) was nitrated, worked up in CCl_4 and the product mixture chromatographed on 10% deactivated alumina. Elution with light petroleum gave 3,4'-dinitro-2,4,6-trimethylbiphenyl as white crystals; m.p. 120° ; n.m.r. (CDCl_3) δ = 1.93 (s, ArCH_3 , 3H), 2.03 (s, ArCH_3 , 3H), 2.32 (s, ArCH_3 , 3H), 7.12 (s, ArH , 1H), quartet centred on 7.85 (ArH , 4H); I.R. (KBr) 1505, 1340, 855, 700 cm^{-1} ; mass spectrum, m/e 286 (M^+) (Found m/e 286.095491. $\text{C}_{15}\text{H}_{14}\text{N}_2\text{O}_4$ requires mol. wt. 286.095349). Elution with 20:1 light petroleum:ether gave 3,4',5-trinitro-2,4,6-trimethylbiphenyl as yellow crystals; m.p. 216° (lit. $216-7^\circ$ ⁷⁷); n.m.r. (CDCl_3) δ = 2.00 (s, ArCH_3 , 6H), 2.23 (s, ArCH_3 , 3H), quartet centred on 7.87 (ArH , 4H); I.R. (KBr) 1540, 1520, 1330, 715 cm^{-1} ; mass spectrum, m/e 331 (M^+) (Found m/e 331.079028. Calc. for $\text{C}_{15}\text{H}_{13}\text{N}_3\text{O}_6$ 331.080427).

2,2',4,4',6,6'-Hexamethoxybiphenyl (1g.) was nitrated and worked up in CCl_4 . Elution with 10:1 light petroleum:ether down a 10% deactivated alumina column gave tetranitrohexamethoxybiphenyl as a viscous yellow oil which could not be crystallised. N.m.r. (CDCl_3) δ = 3.90 (s, ArOCH_3 , 6H), 3.95 (s, ArOCH_3 , 12H); I.R. (smear) 1520, 1330, 1150, 970, 730 cm^{-1} ; mass spectrum, m/e 514 (M^+) (Found m/e 258.048527. $\text{C}_9\text{H}_{10}\text{N}_2\text{O}_7$ requires mol.wt. 258.048792 corresponding to M-

$\text{Ph}(\text{OCH}_3)_3(\text{NO}_2)_2$).

4-Methoxybiphenyl (5g.) was nitrated and worked up by the CCl_4 method. A yellow-orange solid came out of solution as the CCl_4 was being evaporated. This was collected and recrystallised (1:1 pentane:ether) to give 3,5-dinitro-4-methoxybiphenyl as yellow crystals; m.p. 141° (lit. $141-2^\circ$ ⁷⁸); n.m.r. (CCl_4) $\delta = 3.83$ (s, ArOCH_3 , 3H), 6.83 (d, $J=9$ c.p.s., ArH , 2H), multiplet centred at 7.40 (ArH , 5H); I.R. (KBr) 1520, 1320, cm^{-1} ; mass spectrum, m/e 274 (M^+) (Found m/e 274.058887. Calc. for $\text{C}_{13}\text{H}_{10}\text{N}_2\text{O}_5$ 274.058965). Chromatography of the product mixture residue on 10% deactivated alumina gave more of this compound on elution with 36:1 light petroleum:ether. Elution with 25:1 light petroleum:ether gave a trinitromethoxybiphenyl as a viscous yellow oil; mass spectrum, m/e 319 (M^+) (Found m/e 318.983862. $\text{C}_{13}\text{H}_9\text{N}_3\text{O}_7$ requires mol. wt. 318.984033).

4-Bromobiphenyl (5g.) was nitrated, worked up in CCl_4 and the residue adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 3-nitro-4-bromobiphenyl as pale yellow crystals; m.p. 43° (lit. $43.2-43.7^\circ$ ⁷⁹); n.m.r. (CDCl_3) multiplet centred on $\delta = 7.37$; I.R. (KBr) 1515, 1330, 1000 cm^{-1} ; mass spectrum, m/e 279 (M^+) (Found m/e 276.972889. Calc. for $\text{C}_{12}\text{H}_8\text{NO}_2\text{Br}$ ⁷⁹ 276.973889). Elution with 20:1 light petroleum:ether brought through 4'-nitro-4-bromobiphenyl as white crystals; m.p. $175-6^\circ$ (lit.

176° 80); n.m.r. (CDCl₃) multiplet centred at 7.90; I.R. (KBr) 1515, 1325, 825 cm⁻¹; mass spectrum, m/e 279 (M⁺) (Found m/e 276.972635. Calc. for C₁₂H₈NO₂Br⁷⁹ 276.973889).

para-Methoxytoluene (2.5g.) was nitrated and worked up by the CCl₄ method. The resulting yellow oil was adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 3,5-dinitro-4-methoxytoluene as white crystals; m.p. 123° (lit. 123-4° 78); n.m.r. (CDCl₃) δ = 2.50 (s, ArCH₃, 3H), 4.05 (s, ArOCH₃, 3H), 7.84 (s, ArH, 2H); I.R. (KBr) 1525, 1330, 980, 730 cm⁻¹; mass spectrum, m/e 212 (M⁺) (Found m/e 212.043450. Calc. for C₈H₈N₂O₅ 212.043316). Elution with 25:1 light petroleum:ether gave 4-methyl-4-nitrocyclohexa-2,5-dien-1-one as a yellow oil; n.m.r. (CDCl₃) δ = 1.95 (s, ArCH₃, 3H), 5.66 (d, J=10 c.p.s. 2H), 6.53 (d, J=10 c.p.s. 2H) both diene protons; I.R. (smear) 1670, 1635, 1610, 1545, 1365 cm⁻¹; mass spectrum, m/e 153 (M⁺) (Found m/e 153.042865. C₇H₇NO₃ requires mol. wt. 153.042589); ultraviolet (TFE) λ 220nm. ε = 15,700.

para-Bromotoluene (3.5g.) was nitrated and worked up by the CCl₄ method. The resulting yellow oil was adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 3-nitro-4-bromotoluene as white crystals; m.p. 33° (lit. 30.2-31.2° 81); n.m.r. (CCl₄) δ = 2.53 (s, ArCH₃, 3H), 7.10 (s,) and 7.20 (s,) 7.48 (d, J=2 c.p.s.), 7.62 (d, J=2 c.p.s.), all giving two

protons, 7.98 (d, J=2 c.p.s. ArH, 1H); I.R. (nujol) 1540, 1355, 880 cm^{-1} ; mass spectrum, m/e 217 (M^+) (Found m/e 214.958377. Calc. for $\text{C}_7\text{H}_6\text{NO}_2\text{Br}^{79}$ 214.958240). Elution with 32:1 light petroleum:ether gave 4-methyl-4-nitrocyclohexa-2,5-dien-1-one identical with the sample isolated from the nitration of p-methoxytoluene. Elution with 10:1 light petroleum:ether gave 2-nitro-p-cresol as yellow crystals; m.p. 33° (lit. 32° ⁸²); n.m.r. (CDCl_3) δ = 2.35 (s, ArCH₃, 3H), 6.97 (s,), 7.10 (s,), 7.32 (d, J=2 c.p.s.), 7.45 (d, J=2 c.p.s.), all giving two protons, 7.87 (d, J=2 c.p.s. ArH, 1H), 10.57 (s, ArOH, 1H); I.R. (nujol) 3250, 1540, 1355, 825 cm^{-1} ; mass spectrum, m/e 153 (M^+) (Found m/e 153.042584. Calc. for $\text{C}_7\text{H}_7\text{NO}_3$ 153.042589). This compound formed as a result of rearomatisation of some of the dienone on the column. There was also a gum accounting for 12% of the reaction products which was recolumned on 10% deactivated alumina. The only product which could be identified in this mixture of at least three compounds was a dinitro-bromotoluene; mass spectrum, m/e 261 (M^+) (Found m/e 259.943032. Calc. for $\text{C}_7\text{H}_5\text{N}_2\text{O}_4\text{Br}^{79}$ 259.943317). The rest of the gum appeared to consist mainly of dibrominated products.

para-Acetoxytoluene (3g.) was nitrated and worked up by both methods (p.23). The yellow-red oily residue that resulted in each case was adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 3-nitro-

4-acetoxytoluene as a colourless oil; n.m.r. (CDCl_3) $\delta = 2.33$ (s, ArOAc , 3H), 2.42 (s, ArCH_3 , 3H), multiplet centred on 7.33 (2H), 7.95 (s, ArH , 1H); I.R. (smear) $1775, 1535, 1335, 1175 \text{ cm}^{-1}$; mass spectrum, m/e 195 (M^+) (Found m/e 195.053152. $\text{C}_9\text{H}_9\text{NO}_4$ requires mol. wt. 195.052375). Elution with 22:1 light petroleum: ether brought through 4-methyl-4-nitrocyclohexa-2,5-dien-1-one identical with the sample isolated from the nitration of p-methoxytoluene. Elution with 8:1 light petroleum:ether gave 2-nitro-p-cresol identical with the sample isolated from the nitration of p-bromotoluene. The structure of 3-nitro-4-acetoxytoluene was confirmed by hydrolysing with sulphuric acid to give 2-nitro-p-cresol identical with the previously obtained samples. Elution with 36:1 light petroleum:ether gave a mixture of 2-and 3-nitro-4-acetoxytoluene. The presence of the 2-nitro isomer was established by hydrolysing this fraction with sulphuric acid to give 3-nitro-p-cresol (m.p. $78-9^\circ$ lit. 79° ⁸³) as well as 2-nitro-p-cresol.

Acetoxyprehnitene (1g.) was nitrated and worked up by the CCl_4 method. As the solvent was being removed a white solid formed which, after recrystallisation from light petroleum, gave 2,3,4,5-tetramethyl-4-nitrocyclohexa-2,5-dien-1-one as white crystals; m.p. 83° ; n.m.r. (CDCl_3) $\delta = 1.85$ (s, ArCH_3 , 3H), 1.93 (s, ArCH_3 , 6H), 1.95 (s, ArCH_3 , 3H), 6.25 (broad s, diene proton 1H); I.R. (KBr). $1680, 1640, 1540, 1365 \text{ cm}^{-1}$; mass spectrum, m/e

195 (M^+) (Found m/e 195.090384. $C_{10}H_{13}NO_3$ requires mol. wt. 195.089537); ultraviolet (TFE) 237nm. 13,560. This was the only isolated product. The remaining material (<3%) was an intractable gum. The dienone rearranged at room temperature to 2,3,4,5-tetramethyl-o-nitrophenol as white crystals; m.p. 90° ; n.m.r. ($CDCl_3$) δ = 2.15 (s, $ArCH_3$, 3H), 2.25 (s, $ArCH_3$, 3H), 2.33 (s, $ArCH_3$, 3H), 2.40 (s, $ArCH_3$, 3H), 10.40 (s, $ArOH$, 1H); I.R. (KBr) 3300, 1535, 1330 cm^{-1} ; mass spectrum, m/e 195 (M^+) (Found m/e 195.090163. $C_{10}H_{13}NO_3$ requires mol. wt. 195.089537).

5-Fluorohemimellitene (3g.) was nitrated and worked up in CCl_4 . The residue was chromatographed on a 10% deactivated alumina column. Elution with light petroleum gave 4-nitro-5-fluorohemimellitene as white crystals; m.p. $38-9^\circ$; n.m.r. ($CDCl_3$) δ = 2.15 (s, $ArCH_3$, 3H), 2.20 (s, $ArCH_3$, 3H), 2.27 (s, $ArCH_3$, 3H), 6.83 (d, $J=10$ c.p.s., ArH , 1H); I.R. (KBr) 1530, 1345, 1080 cm^{-1} ; mass spectrum m/e 183 (M^+) (Found m/e 183.070010. $C_9H_{10}NO_2F$ requires mol. wt. 183.069551). Elution with 36:1 light petroleum:ether gave 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one identical with an authentic sample¹³. Elution with 2:1 light petroleum:ether brought through 3,4,5-trimethyl-o-nitrophenol identical with an authentic sample.

5-Bromopseudocumene (5g.) was nitrated and worked up by both methods (p.23). The pumpdown gave a red

oil containing 2,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one which was obtained in 80% purity by elution with light petroleum down a 10% deactivated alumina column. It had n.m.r. (CCl_4) $\delta = 1.78$ (s, ArCH_3 , 3H), 1.83 (s, ArCH_3 , 3H), 1.87 (s, ArCH_3 , 3H), 6.04 (q, $J=1.5$ c.p.s., diene proton, 1H), 6.48 (q, $J=1.5$ c.p.s., diene proton, 1H); I.R. (smear) 1680, 1650, 1550, 1360 cm^{-1} ; mass spectrum, m/e 181 (M^+) (Found m/e 181.074121. $\text{C}_9\text{H}_{11}\text{NO}_3$ requires mol. wt. 181.073887). Elution with 25:1 light petroleum: ether gave 3 or 6-nitro-5-bromopseudocumene as white crystals; m.p. $161-2^\circ$; n.m.r. (CCl_4) $\delta = 2.25$ (s, ArCH_3 , 3H), 2.33 (s, ArCH_3 , 3H), 2.40 (s, ArCH_3 , 3H), 7.07 (s, ArH , 1H); I.R. (KBr) 1535, 1330, 830 cm^{-1} ; mass spectrum, m/e 245 (M^+) (Found m/e 244.989354. $\text{C}_9\text{H}_{10}\text{NO}_2\text{Br}^{81}$ requires mol. wt. 244.987569).

2,4,5-Trimethyl-4-nitrocyclohexa-2,5-dien-1-one decomposed at 0° in eight hours to give two products which were separated by chromatography on 10% deactivated alumina. Elution of the decomposition products with light petroleum gave 2,4,5-trimethyl-o-nitrophenol as orange crystals; m.p. $41-3^\circ$; n.m.r. (CCl_4) $\delta = 2.20$ (s, ArCH_3 , 6H), 2.34 (s, ArCH_3 , 3H), 7.04 (s, ArH , 1H), 9.45 (s, ArOH , 1H); I.R. (KBr) 3450, 1530, 1315, 1240 cm^{-1} ; mass spectrum, m/e 181 (M^+) (Found m/e 181.073894. $\text{C}_9\text{H}_{11}\text{NO}_3$ requires mol. wt. 181.073887). Elution with 25:1 light petroleum:ether gave 2,5-dimethyl-4-hydroxy-phenylnitromethane as yellow crystals; m.p. $97-9^\circ$;

n.m.r. (CDCl_3) δ = 2.33 (s, ArCH_3 , 3H), 2.52 (s, ArCH_3 , 3H), 5.47 (s, ArCH_2NO_2 , 2H), 7.39 (s, ArH , 1H), 7.56 (s, ArH , 1H), 9.77 (s, ArOH , 1H); I.R. (KBr) 3450, 1540, 1360, 1180 cm^{-1} ; mass spectrum, m/e 181 (M^+) (Found m/e 181.073741.

$\text{C}_9\text{H}_{11}\text{NO}_3$ requires mol. wt. 181.073887). To establish the position of the side-chain nitro group, this compound was oxidised by the method of Schechter and Williams⁶⁶ to give 2,5-dimethyl-4-hydroxybenzaldehyde; m.p. 132° (lit. 133°⁸⁴), hydrazone m.p. 161° (lit. 163°⁸⁴). The isomeric 2,4-dimethyl-5-hydroxybenzaldehyde has m.p. 115°⁸⁵. The ratio of these decomposition products was ten parts nitrophenol to one part nitrophenylmethane.

3,4,5-Trimethylacetanilide (3.5g.) was nitrated, worked up in CCl_4 and the residue adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 2-nitro-3,4,5-trimethylacetanilide as orange crystals; m.p. 176-9°; n.m.r. (CDCl_3) δ = 2.10 (s, ArNHCOCH_3 , 3H), 2.16 (s, ArCH_3 , 6H), 2.21 (s, ArCH_3 , 3H), 6.33 (s, ArNHCOCH_3 , 1H), 7.15 (s, ArH , 1H); I.R. (KBr) 3400, 1680, 1540, 1360, 1085 cm^{-1} ; mass spectrum, m/e 222 (M^+) (Found m/e 222.101026. $\text{C}_{11}\text{H}_{14}\text{N}_2\text{O}_3$ requires mol. wt. 222.100435). Elution with 38:1 light petroleum:ether gave 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one, identical with an authentic sample¹³.

ortho-Xylene (5g.) was nitrated using nitric acid (1 ml.) in propionic anhydride (10 ml.). The CCl_4

work-up was used and the oil adsorbed onto 10% deactivated alumina. Elution with light petroleum gave 4-propionoxy-o-xylene as white crystals; m.p. $33-4^{\circ}$; n.m.r. (CCl_4) $\delta = 1.25$ (t, $J=8$ c.p.s. $\text{ArOCOCH}_2\text{CH}_3$, 3H), 2.26 (s, ArCH_3 , 6H), 2.64 (q, $J=8$ c.p.s. $\text{ArOCOCH}_2\text{CH}_3$, 2H), 7.15, 7.48 (both d, $J=8$ c.p.s. ArH , each 1H), 7.25 (s, ArH , 1H); I.R. (smear) 1770, 1120 cm^{-1} ; mass spectrum m/e 178 (M^+) (Found m/e 178.099214. $\text{C}_{11}\text{H}_{14}\text{O}_2$ requires mol. wt. 178.099373). This structure was established by hydrolysis to give 3,4-o-xylenol identical with an authentic sample. Further elution with light petroleum gave 3-nitro-o-xylene as a liquid which solidified on standing at 0° ; b.p. 240° (lit. $120-5^{\circ}/10-12\text{mm}^{86}$) identical with an authentic sample. Elution with 36:1 light petroleum:ether gave 4-nitro-o-xylene as white crystals; m.p. 28° (lit. 28.5°^{87}) identical with an authentic sample.

para-Bromoethylbenzene (5 g.) was nitrated and worked up in carbon tetrachloride. The residue was chromatographed on both 10% deactivated alumina and then silica gel but none of the products was isolated in a pure state. Elution with light petroleum down the alumina column gave a 60:40 mixture of mononitro-p-bromoethylbenzene; (Found m/e 228.974106. Calc. for $\text{C}_8\text{H}_8\text{NO}_2\text{Br}^{79}$ 228.973889) and a dinitro-p-bromoethylbenzene; (Found m/e 273.959344. Calc. for $\text{C}_8\text{H}_7\text{N}_2\text{O}_4\text{Br}^{79}$ 273.958967). Elution with 100:1 light petroleum:ether gave a mixture of a dibromonitro-ethylbenzene; (Found

m/e 306.884031. $C_8H_7NO_2Br_2^{79}$ requires mol. wt. 306.884455), an acetoxy-bromoethylbenzene; (Found m/e 241.993724. $C_{10}H_{11}O_2Br^{79}$ requires mol. wt. 241.994289) and a compound with m/e 167.059061. $C_8H_9NO_3$ requires mol. wt. 167.058238 suggesting this compound was either 4-ethyl-4-nitrocyclohexa-2,5-dien-1-one or the corresponding nitrophenol decomposition product. G.l.c. analysis of the product mixture indicated eight products in all.

Competitive nitrations

The competitive nitrations were carried out by taking an equimolar mixture of the two reactants being investigated and adding an amount of nitrating agent (nitric acid-acetic anhydride at 0°) less than the stoichiometric amount. The reaction mixture was then analysed by n.m.r. at 0° to 3° at various stages of reaction. Allowance was made for the fact that some of the competing compounds underwent ipso-nitration to different degrees. G.l.c. analysis of the final product mixture from the competition nitrations between acetoxy-hemimellitene and hemimellitene and between bromo- and acetoxyhemimellitene showed the ratio of normal:ipso nitration products was the same as that obtained when each was nitrated individually. The same was assumed to apply in the other cases. The major error in an n.m.r. analysis lay in an accurate reading of the

integral of the reactant's aromatic proton signals. This introduced approximately 10% error into the measurements.

Determination of the rearomatisation mechanism of two nitrocyclohexadienones

The two dienones studied were 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one and 3,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-one. These were prepared by well known methods¹³ from 5-acetoxymellitene and 4-acetoxym-xylene respectively. In a typical decomposition run the dienone (20mg.) with N¹⁴ or N¹⁵ enriched sodium nitrite (8mg.) was dissolved in methanol (0.5 ml.) and allowed to rearrange at room temperature. The reactions were carried out in sealed n.m.r. tubes and followed by n.m.r. The N¹⁵ enrichment in the rearrangement product (nitrophenol) was calculated from the mass spectra of the nitrophenol by comparison of the height of the m+1 peak for a reaction run in the presence of NaN¹⁵O₂ with the height of the m+1 peak for a reaction run in the presence of NaN¹⁴O₂. Thus all the reactions were run in pairs and repeated several times to allow for variations in machine response.

Kinetic runs were carried out to determine the order of reaction with respect to both dienone and sodium nitrite. These reactions were also monitored by n.m.r. In these runs an internal, inert standard

(p-dichlorobenzene) was used. This had a single n.m.r. signal, well downfield from the dienone-phenol region, which was used to measure concentrations of the reacting species during reaction. Each kinetic run was carried out several times to allow for variations in n.m.r. response.

R E S U L T S

Product distributions

The product ratios given here are those determined by g.l.c. analysis after work-up of the reaction mixture and are all averages over a number of runs.

(1) Nitration of para-diethylbenzene with nitric acid-acetic anhydride.

4-(α -nitroethyl)-ethylbenzene	55 \pm 4%
2-nitro-1,4-diethylbenzene	35 \pm 3%
2-acetoxy-1,4-diethylbenzene	7 \pm 1%
<u>p</u> -diethylbenzene	3 \pm 1%

(2) Nitration of para-ethyltoluene with nitric acid-acetic anhydride.

4-(α -nitroethyl)-toluene	35 \pm 3%
4-ethyl-phenylnitromethane	30 \pm 3%
2-nitro-4-ethyltoluene	18 \pm 2%
3-nitro-4-ethyltoluene	14 \pm 2%
2-acetoxy-4-(α -nitroethyl)-toluene	2 \pm 1%
3-acetoxy-4-ethyltoluene	\sim 1%

(3) Nitration of ethylmesitylene with nitric acid-acetic anhydride

3,5-dimethyl-4-ethyl-phenylnitromethane	>98%
nitroethylmesitylene	< 2%

(4) Nitration of bromomesitylene with nitric acid-acetic anhydride

2,4-dibromo-6-nitromesitylene	45 \pm 4%
nitromesitylene	41 \pm 3%
nitrobromomesitylene	14 \pm 2%

(5) Nitration of 2,4,6-trimethoxybromobenzene with nitric acid-acetic anhydride

2,4,6-trimethoxynitrobenzene	48 \pm 4%
1,3-dibromo-5-nitro-2,4,6-trimethoxybenzene	22 \pm 2%
nitro-2,4,6-trimethoxybromobenzene	20 \pm 2%
1,3,5-tribromo-2,4,6-trimethoxybenzene	10 \pm 2%

(6) Nitration of chloromesitylene with nitric acid-acetic anhydride

nitrochloromesitylene	78 \pm 4%
3,5-dimethyl-4-chloro-phenylnitromethane	20 \pm 2%
dinitrochloromesitylene	\sim 2%

(7) Nitration of 2,4,6-trimethoxychlorobenzene with nitric acid-acetic anhydride

3-nitro-2,4,6-trimethoxychlorobenzene	75 \pm 4%
4-chloro-3,5-dimethoxy-2-nitrophenol	25 \pm 2%

(8) Nitration of fluoromesitylene with nitric acid-acetic anhydride

nitrofluoromesitylene	95 \pm 4%
dinitrofluoromesitylene	5 \pm 1%

(9) Nitration of 2,4,6-trimethoxyfluorobenzene
with nitric acid-acetic anhydride

nitro-2,4,6-trimethoxyfluorobenzene > 95%

other < 5%

(10) Nitration of methoxymesitylene with nitric
acid-acetic anhydride

3,5-dimethyl-4-methoxy-phenylnitromethane $60 \pm 4\%$

mesitol $29 \pm 3\%$

2-acetoxy-3,5-dimethyl-4-methoxy-

phenylnitromethane $11 \pm 2\%$

(11) Nitration of 2,4,6-trimethylbiphenyl with
nitric acid-acetic anhydride

3,4'-dinitro-2,4,6-trimethylbiphenyl $70 \pm 5\%$

3,4',5-trinitro-2,4,6-trimethylbiphenyl $30 \pm 5\%$

(12) Nitration of 2,2',4,4',6,6'-hexamethoxybiphenyl
with nitric acid-acetic anhydride

2,2',4,4',6,6'-hexamethoxy-3,3',5,5'-

tetranitrobiphenyl 100%

(13) Nitration of 4-methoxybiphenyl with nitric
acid-acetic anhydride

3,5-dinitro-4-methoxybiphenyl $\sim 95\%$

trinitro-methoxybiphenyl $\sim 5\%$

(14) Nitration of 4-bromobiphenyl with nitric acid-
acetic anhydride

4'-nitro-4-bromobiphenyl $90 \pm 5\%$

3-nitro-4-bromobiphenyl $10 \pm 2\%$

(15) Nitration of para-methoxytoluene with nitric acid-acetic anhydride

3,5-dinitro-4-methoxytoluene	80 \pm 5%
2-nitro- <u>p</u> -cresol	20 \pm 5%

(16) Nitration of para-bromotoluene with nitric acid-acetic anhydride

3-nitro-4-bromotoluene	48 \pm 4%
2-nitro- <u>p</u> -cresol	40 \pm 4%
other, containing a dinitro-bromotoluene	12 \pm 2%

(17) Nitration of para-acetoxytoluene with nitric acid-acetic anhydride

2-nitro- <u>p</u> -cresol	50 \pm 5%
2-nitro-4-acetoxytoluene	\sim 30%
3-nitro-4-acetoxytoluene	\sim 20%

(18) Nitration of acetoxyprehnitene with nitric acid-acetic anhydride

2,3,4,5-tetramethyl- <u>o</u> -nitrophenol	> 97%
other	< 3%

(19) Nitration of 5-fluorohemimellitene with nitric acid-acetic anhydride

3,4,5-trimethyl- <u>o</u> -nitrophenol	67 \pm 3%
4-nitro-5-fluorohemimellitene	33 \pm 2%

(20) Nitration of 5-bromopseudocumene with nitric acid-acetic anhydride

3,4,5-trimethyl- <u>o</u> -nitrophenol	78 ± 3%
3 or 6-nitro-5-bromopseudocumene	15 ± 2%
2,5-dimethyl-4-hydroxy-phenylnitromethane	7 ± 1%

(21) Nitration of 3,4,5-trimethylacetanilide with nitric acid-acetic anhydride

3,4,5-trimethyl- <u>o</u> -nitrophenol	55 ± 4%
2-nitro-3,4,5-trimethylacetanilide	45 ± 4%

(22) Nitration of ortho-xylene with nitric acid-propionic anhydride

4-propionoxy- <u>o</u> -xylene	50 ± 3%
4-nitro- <u>o</u> -xylene	35 ± 3%
3-nitro- <u>o</u> -xylene	15 ± 2%

(23) Nitration of para-bromoethylbenzene with nitric acid-acetic anhydride

The product mixture contained eight compounds including a mononitro-bromoethylbenzene, a dinitro-bromoethylbenzene, a dibromonitro-ethylbenzene, an acetoxy-bromoethylbenzene and 4-ethyl-4-nitrocyclohexa-2,5-dien-1-one (or the corresponding nitrophenol).

Composition of reaction mixtures by n.m.r.

In each of the following tables (I - VI) there is an error of ± 3 in each figure due to the inaccuracies in estimating the n.m.r. integrals.

Table I

N.m.r. analysis of para-diethylbenzene reaction ($\text{HNO}_3/\text{Ac}_2\text{O}$) before work-up

<u>Product</u>	<u>In reaction mixture before heating</u>	<u>After heating</u>
4-(α -nitroethyl)-ethylbenzene	53	53
2-nitro-1,4-diethylbenzene	32	32
p-diethylbenzene	5	8
2-acetoxy-1,4-diethylbenzene	-	7
dienes	10	-

Table II

N.m.r. analysis of 2,4,6-trimethoxychlorobenzene reaction ($\text{HNO}_3/\text{Ac}_2\text{O}$) before work-up

<u>Product</u>	<u>In reaction mixture before heating</u>	<u>After heating</u>
3-nitro-2,4,6-trimethoxy-chlorobenzene	75	75
4-chloro-3,5-dimethoxy-2-nitrophenol	4	25
dienone	21	-

Table III

N.m.r. analysis of methoxymesitylene reaction ($\text{HNO}_3/\text{Ac}_2\text{O}$)
before work-up

<u>Product</u>	<u>In reaction mixture before heating</u>	<u>After heating to 150°</u>
3,5 -dimethyl-4-methoxy- phenylnitromethane	60	60
mesitol	-	28
2-acetoxy-3,5-dimethyl- 4-methoxyphenylnitro- methane	10	12
dienone	30	-

Table IV

N.m.r. analysis of para-acetoxytoluene reaction
($\text{HNO}_3/\text{Ac}_2\text{O}$) before work-up

<u>Product</u>	<u>In reaction mixture before heating</u>	<u>After heating</u>
2 and 3-nitro-4-acetoxy- toluene	50	50
2-nitro-p-cresol	3	50
dienone	47	-

Table V

N.m.r. analysis of 5-fluorohemimellitene reaction

(HNO₃/Ac₂O) before work-up

<u>Product</u>	<u>In reaction mixture before heating</u>	<u>After heating</u>
4-nitro-5-fluorohemi- mellitene	33	35
3,4,5-trimethyl- <u>o</u> -nitro- phenol	5	65
dienone	62	-

Table VI

N.m.r. analysis of 5-bromopseudocumene reaction

(HNO₃/Ac₂O) before work-up

<u>Product</u>	<u>In reaction mixture before heating</u>	<u>After heating</u>
3 or 6-nitro-5-bromo- pseudocumene	12	15
2,4,5-trimethyl- <u>o</u> -nitro- phenol	8	78
2,5-dimethyl-4-hydroxy- phenylnitromethane	-	7
dienone	80	-

Table VII

Product distribution from nitration of 4-acetoxy-o-xylene

	<u>In HNO₃/Ac₂O</u>	<u>In HNO₃/Pr₂O</u>
dienone	67%	70%
nitro-4-acetoxy- <u>o</u> -xylenes	33%	30%

Product distribution from nitration of 5-acetoxyhemi-mellitene

	<u>In HNO₃/Ac₂O</u>	<u>In HNO₃/Pr₂O</u>
dienone	72%	70%
4-nitro-5-acetoxyhemi-mellitene	28%	30%

Product distribution from nitration of o-xylene

	<u>In HNO₃/Ac₂O</u>	<u>In HNO₃/Pr₂O</u>
4-acetoxy- <u>o</u> -xylene	50%	-
4-propionoxy- <u>o</u> -xylene	-	50%
4-nitro- <u>o</u> -xylene	36%	35%
3-nitro- <u>o</u> -xylene	14%	15%

Table VIII

Diene and dienone rearrangement products

Compound	Rearrangement conditions.	Product(s)
1,4-diethyl-1-acetoxy-4-nitrocyclohexa-2,5-diene	acetic acid at 30°	2-acetoxy-1,4-diethylbenzene (70%) p-diethylbenzene (30%)
3,5-dimethoxy-4-chloro-4-nitrocyclohexa-2,5-dien-1-one	standing, 25°	4-chloro-3,5-dimethoxy-2-nitrophenol
2,4,6-trimethyl-4-nitrocyclohexa-2,5-dien-1-one	heating to 150°	mesitol
4-methyl-4-nitrocyclohexa-2,5-dien-1-one	standing, 25°	2-nitro-p-cresol
2,3,4,5-tetramethyl-4-nitrocyclohexa-2,5-dien-1-one	standing, 25°	2,3,4,5-tetramethyl-o-nitrophenol
2,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one	CCl ₄ , 0°	2,4,5-trimethyl-o-nitrophenol (91%) 2,5-dimethyl-4-hydroxyphenyl-nitromethane (9%)

Table IX

Product distributions obtained from the competition nitration between acetoxyhemimellitene and bromohemimellitene

<u>Compound</u>	<u>Nitration in isolation</u>		<u>Nitration in competition</u>	
5-acetoxyhemimellitene	dienone	72%	dienone	70%
	4-nitro-5-acetoxyhemimellitene	28%	4-nitro-5-acetoxyhemimellitene	30%
5-bromohemimellitene	dienone	65%	dienone	65%
	4-nitro-5-bromohemimellitene	35%	4-nitro-5-bromohemimellitene	35%

Table X

Product distributions obtained from the competition nitration between acetoxyhemimellitene and hemimellitene

<u>Compound</u>	<u>Nitration in isolation</u>		<u>Nitration in competition</u>	
5-acetoxyhemimellitene	dienone	72%	dienone	70%
	4-nitro-5-acetoxyhemimellitene	28%	4-nitro-5-acetoxyhemimellitene	30%
hemimellitene	diene	38 %	diene	35%
	nitrohemimellitenes	62 %	nitrohemimellitenes	65%

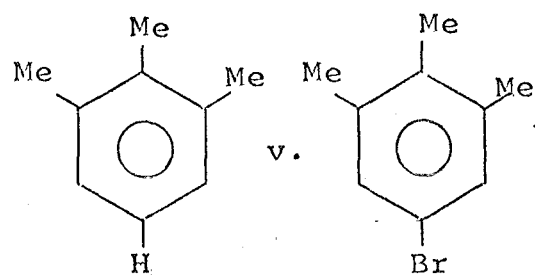
Table XI

Competition nitrations

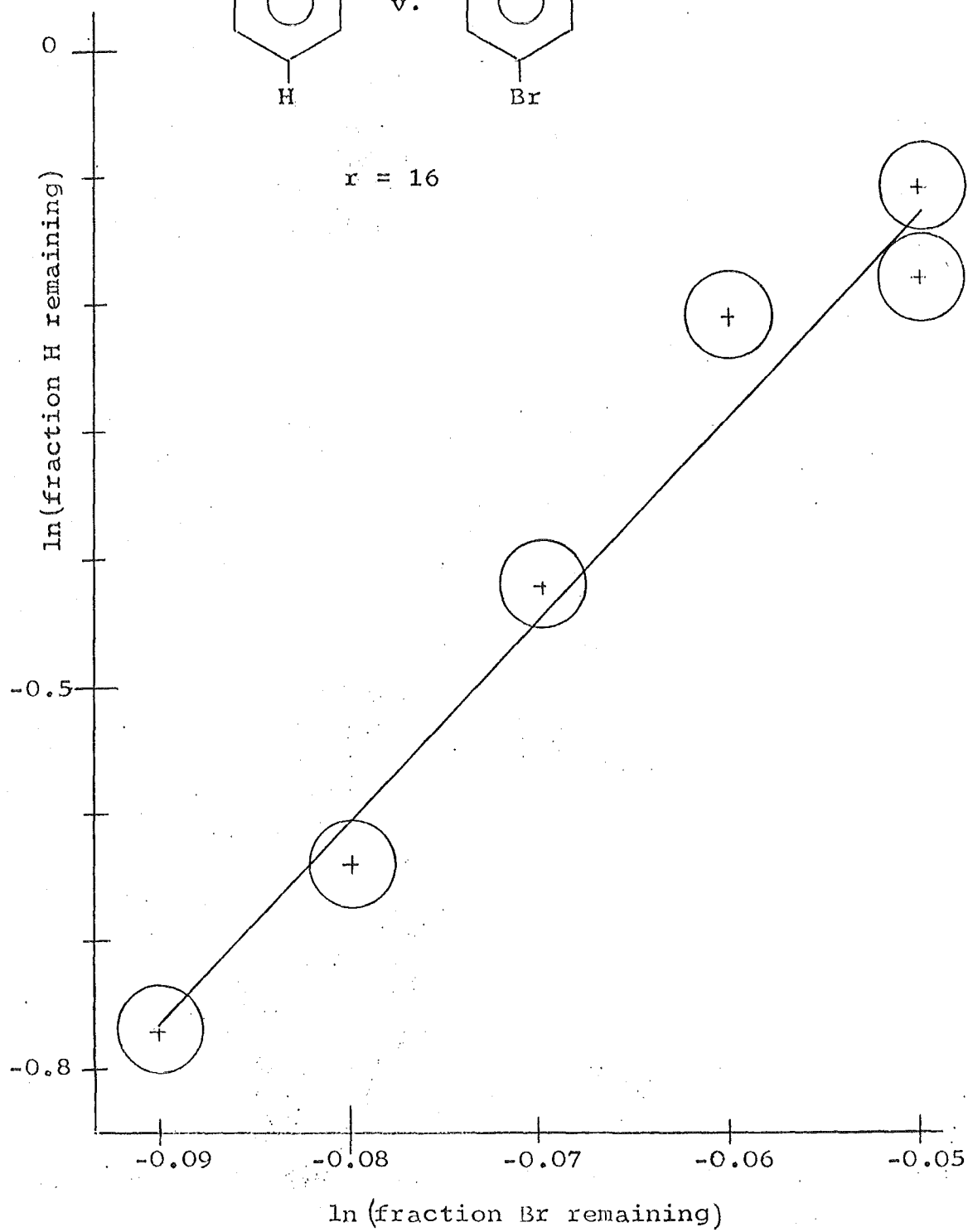
<u>competing reagents</u>		<u>r</u> *
4-acetoxy- <u>o</u> -xylene	v	4-acetoxytoluene >30
5-acetoxyhemimellitene	v	4-acetoxy- <u>o</u> -xylene >30
5-bromohemimellitene	v	4-bromo- <u>o</u> -xylene >30
acetoxyprehnitene	v	5-acetoxyhemimellitene 7
hemimellitene	v	5-acetoxyhemimellitene 18
hemimellitene	v	5-bromohemimellitene 16
5-fluorohemimellitene	v	hemimellitene 10
5-bromohemimellitene	v	5-acetoxyhemimellitene 1

* r is the ratio of first order rate constants. In each case the compound in the left hand column is the more reactive.

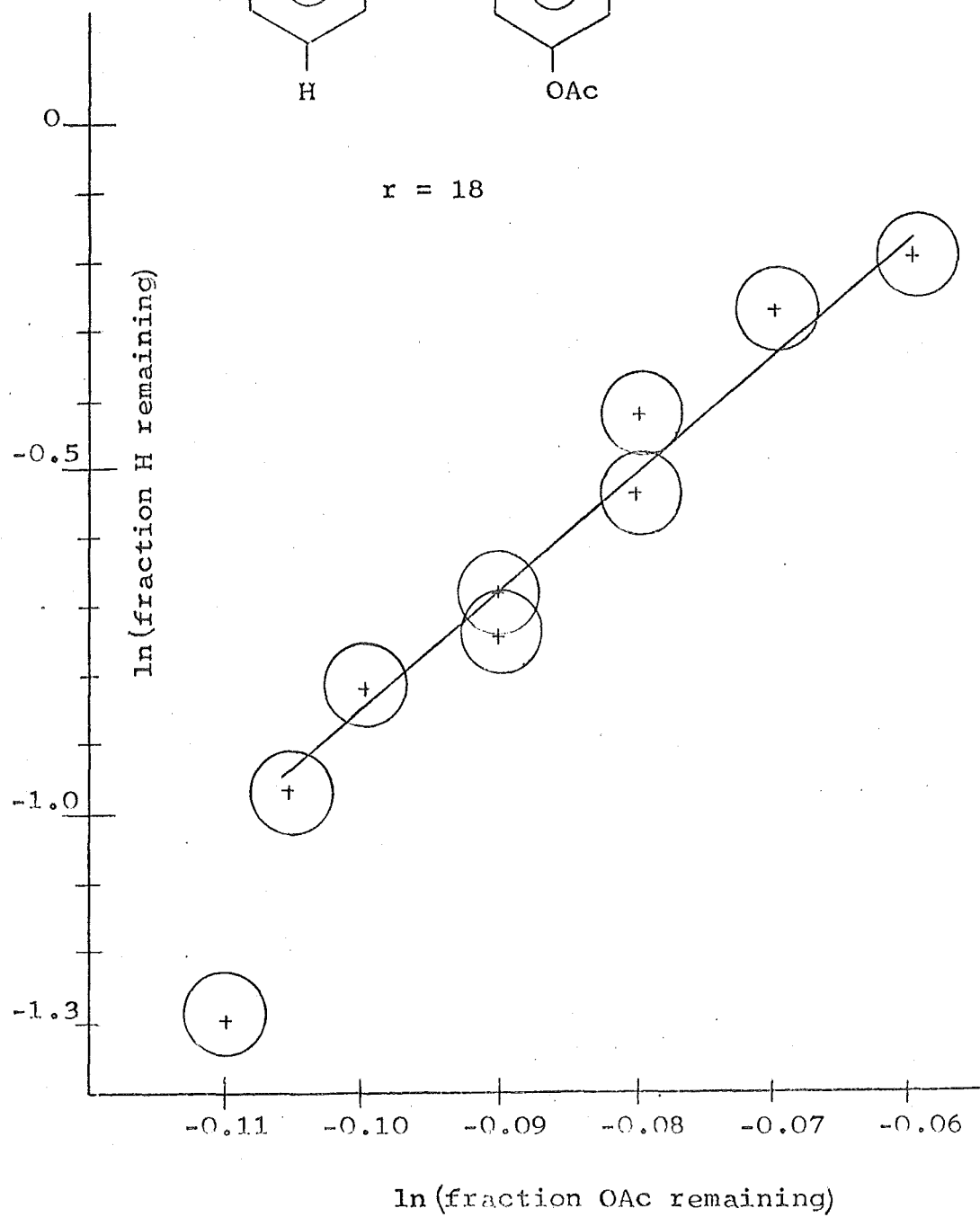
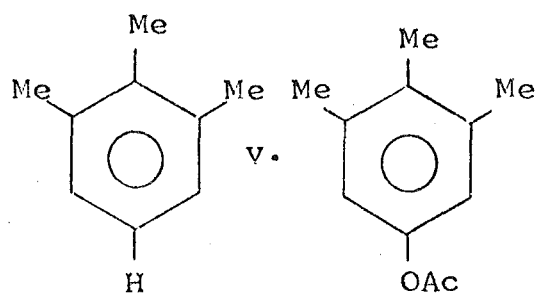
Competition nitration:



$r = 16$



Competition nitration:



Competition nitration:

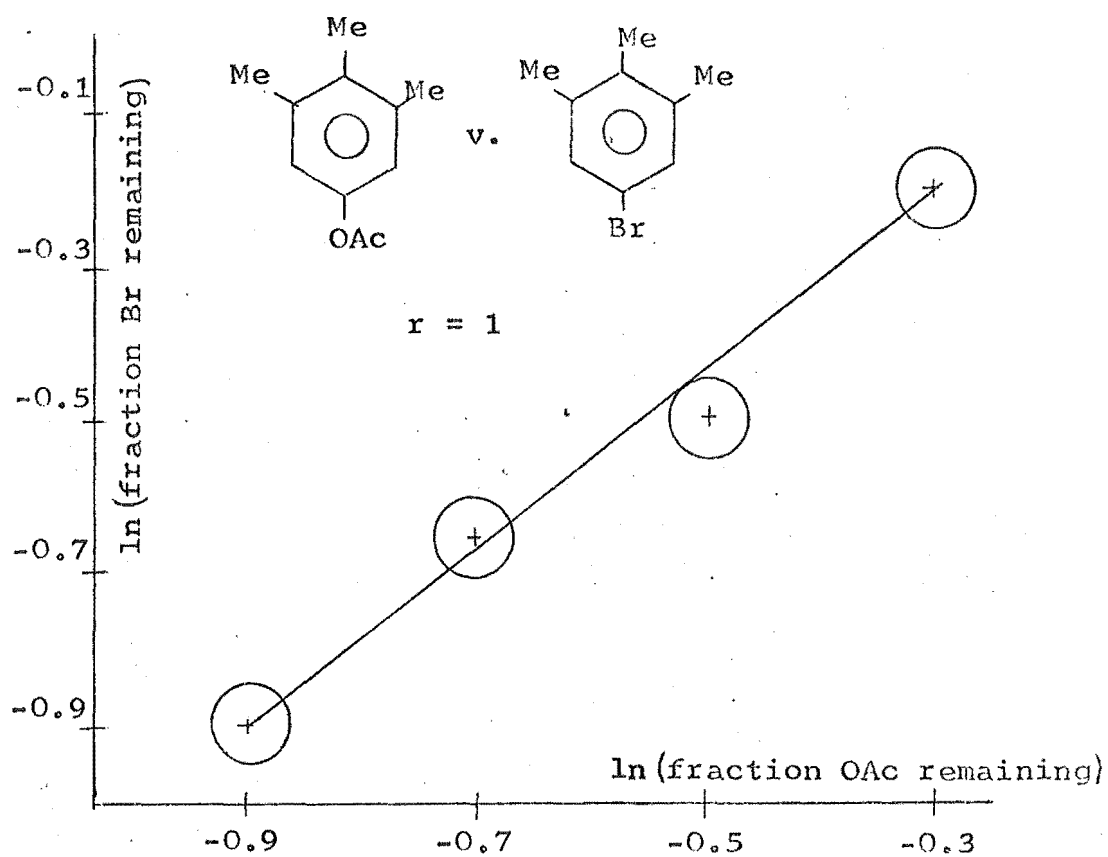
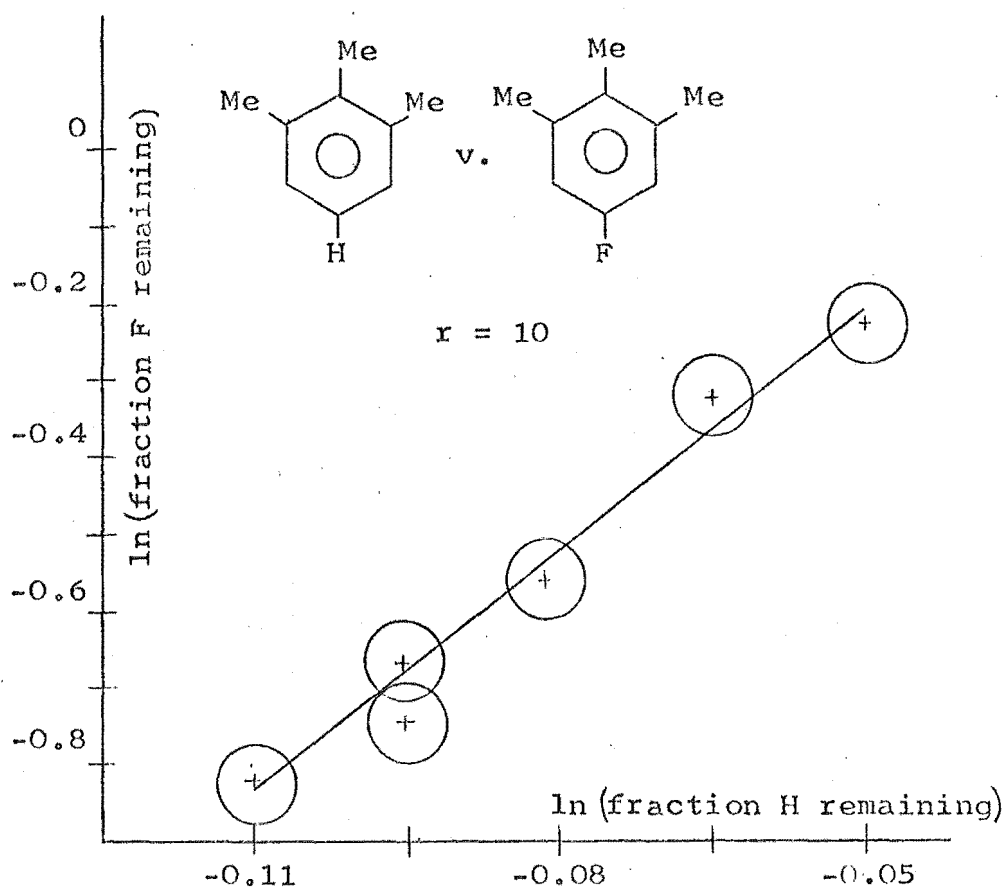


Table XII

Rearomatisation of 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one. Mass spectra of the nitrophenol product.
 [dienone] = [sodium nitrite] = 0.22 mol.l⁻¹

N ¹⁴		N ¹⁵		N ¹⁵ /N ¹⁴ *
Height 181 peak	Height 182 peak	Height 181 peak	Height 182 peak	
10.50	1.10	14.90	4.25	0.18
9.80	1.00	13.25	3.70	0.18
9.50	1.00	9.00	2.50	0.17
8.80	1.00	16.50	4.70	0.17
8.95	1.00	8.60	2.50	0.18
9.50	1.00	9.50	2.60	0.17

* The N¹⁵/N¹⁴ ratio refers to the proportion of N¹⁵ enriched nitrophenol in the product and not to the proportion of available N¹⁵ incorporated.

Table XIII

Rearomatisation of 3,4,5-trimethyl-4-nitrocyclohexa-
2,5-dien-1-one

[dienone] = 0.22 mol.l⁻¹. [sodium nitrite] = 0.44 mol.l⁻¹

N ¹⁴		N ¹⁵		N ¹⁵ /N ¹⁴ ratio
Height 181 peak	Height 182 peak	Height 181 peak	Height 182 peak	
10.00	1.00	17.70	5.70	0.22
15.00	1.60	10.25	3.55	0.24
11.50	1.10	17.50	6.00	0.24
11.70	1.20	14.80	5.20	0.25

Table XIV

Rearomatisation of 3,4,5-trimethyl-4-nitrocyclohexa-
2,5-dien-1-one

[dienone] = 0.22 mol.l⁻¹. [sodium nitrite] = 0.11 mol.l⁻¹

N ¹⁴		N ¹⁵		N ¹⁵ /N ¹⁴ ratio
Height 181 peak	Height 182 peak	Height 181 peak	Height 182 peak	
10.10	1.00	13.20	2.60	0.10
11.05	1.05	15.70	3.22	0.11

Table XV

Rearomatisation of 3,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-one

[dienone] = 0.23 mol.l⁻¹. [sodium nitrite] = 0.23 mol.l⁻¹

N ¹⁴		N ¹⁵		N ¹⁵ /N ¹⁴ ratio
Height 167 peak	Height 168 peak	Height 167 peak	Height 168 peak	
13.20	1.40	11.40	6.05	0.42
28.40	2.75	27.50	13.20	0.42
10.00	1.00	33.00	16.50	0.40
10.40	1.00	20.00	9.85	0.40
13.25	1.45	17.10	7.85	0.42

Table XVI

Rearomatisation of 3,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-one

[dienone] = 0.23 mol.l⁻¹. [sodium nitrite] = 0.46 mol.l⁻¹

N ¹⁴		N ¹⁵		N ¹⁵ /N ¹⁴ ratio
Height 167 peak	Height 168 peak	Height 167 peak	Height 168 peak	
12.50	1.20	19.75	10.00	0.46
8.75	0.90	19.70	11.00	0.46
9.70	1.00	15.80	8.00	0.46

Table XVII

Rearomatisation of 3,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-one

[dienone] = 0.23 mol.l⁻¹. [sodium nitrite] = 0.115 mol.l⁻¹

N ¹⁴		N ¹⁵		N ¹⁵ /N ¹⁴ ratio
Height 167 peak	Height 168 peak	Height 167 peak	Height 168 peak	
21.30	2.30	11.00	3.50	0.21
15.40	1.60	24.50	8.25	0.22
10.00	1.00	13.60	4.20	0.21

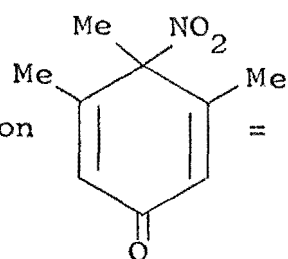
For a rearomatisation of 3,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-one run with [dienone] = 0.23 mol.l⁻¹ and [sodium nitrite] = 0.23 mol.l⁻¹, it was found that both the rearomatisation products, 6-nitro-3,4-xylenol and 2-nitro-3,4-xylenol, had N¹⁵/N¹⁴ ratios of 0.42. The product ratio of the 6-nitrophenol to 2-nitrophenol was not constant, varying between 4:1 and 2:1.

Kinetic studies on the decomposition of 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one and 3,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-one

The rate of rearomatisation of both dienones was shown to be first order in dienone by linear plots of $\ln(A_0 - x)$ against time where A_0 is the initial concentration of dienone and x is the decrease in dienone

/Contd. p. 62

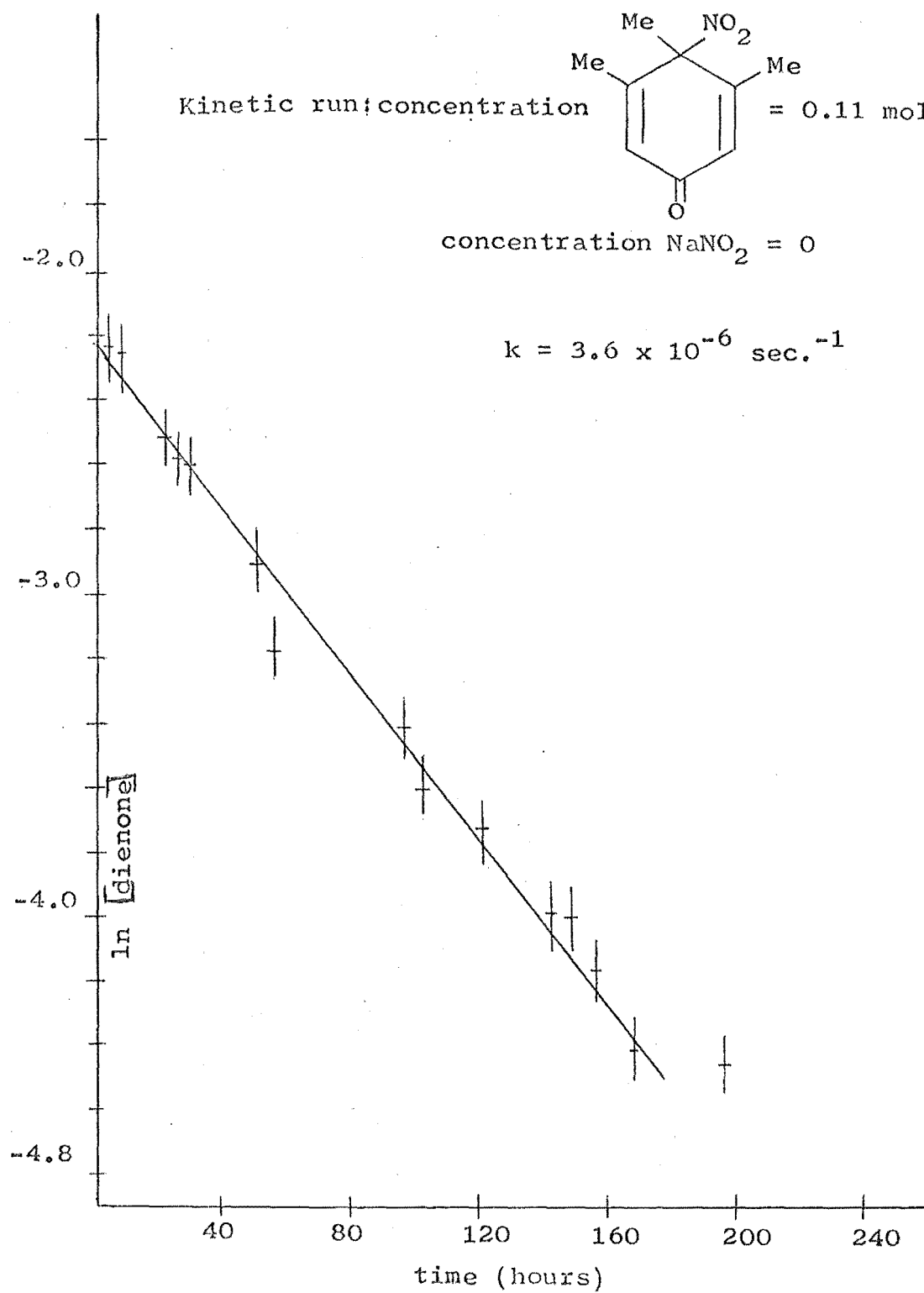
Kinetic run; concentration

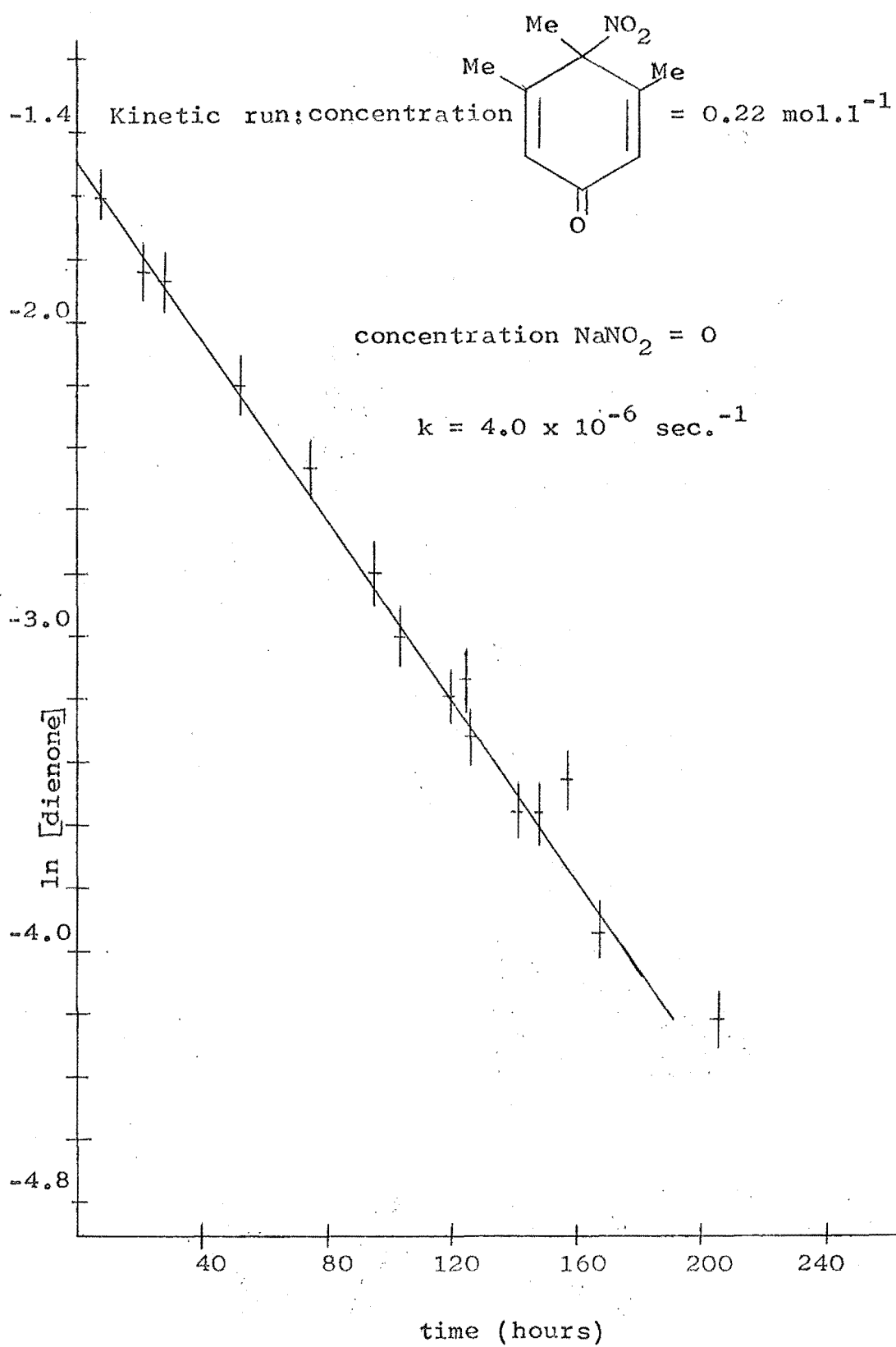


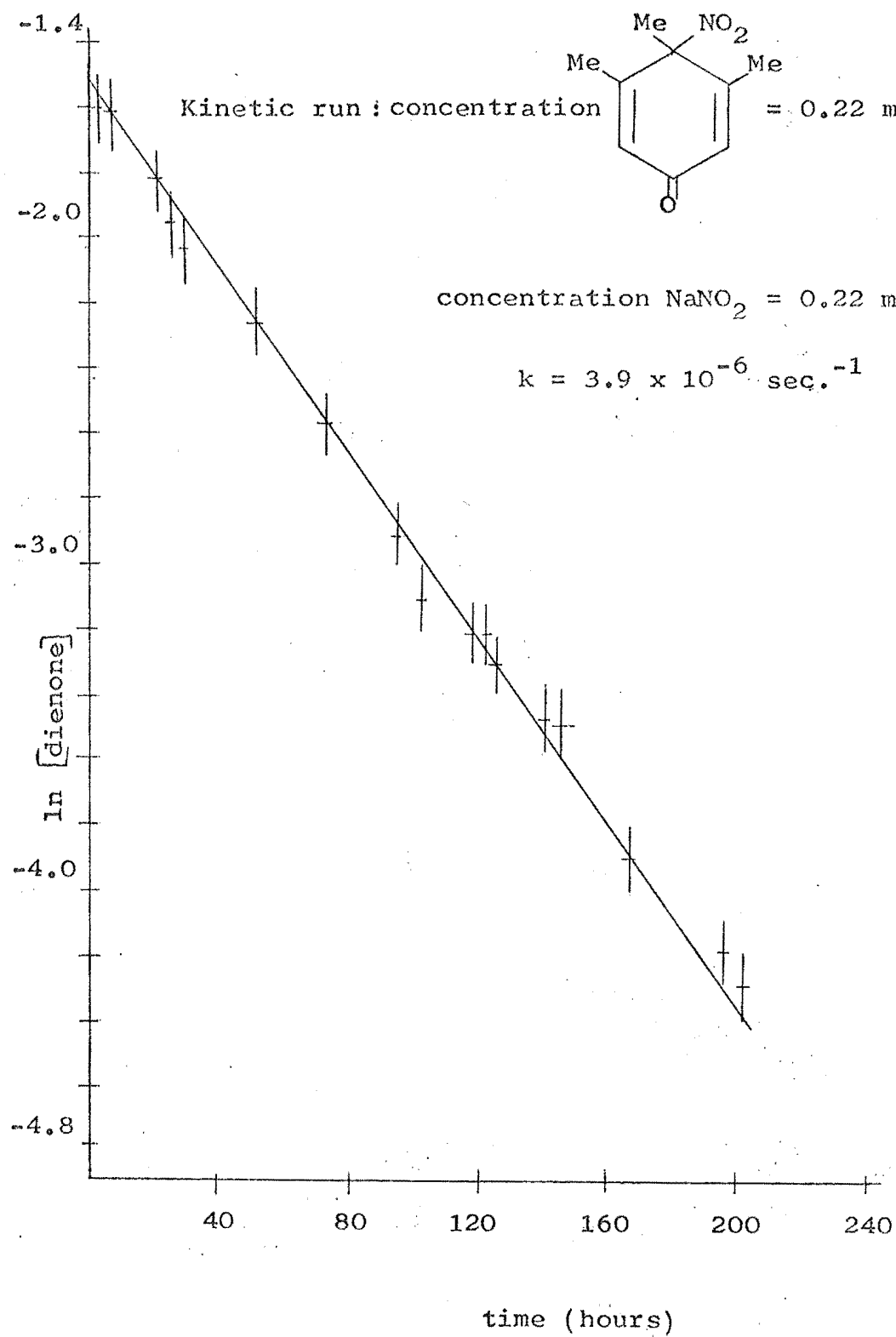
= 0.11 mol.l⁻¹

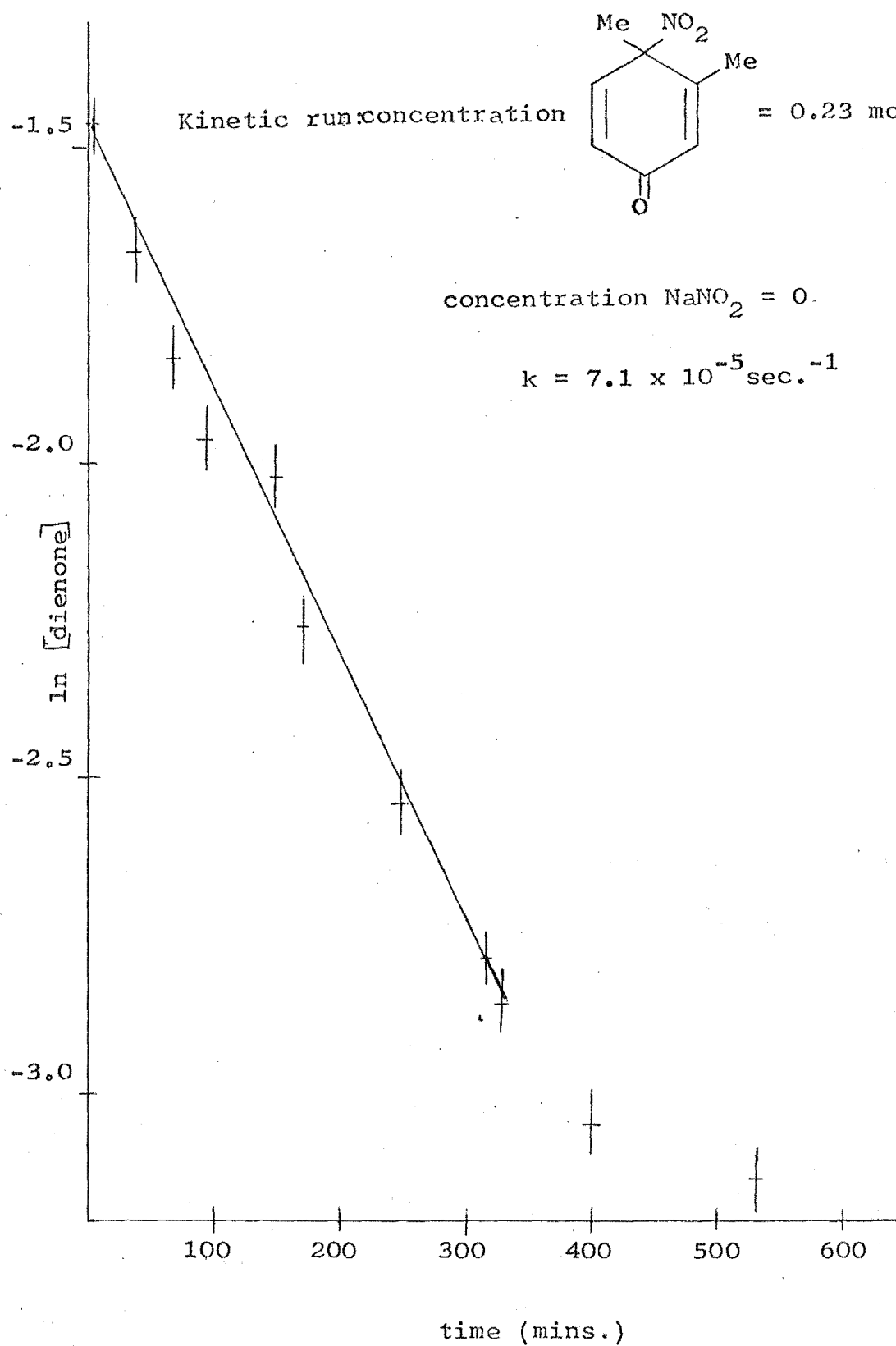
concentration NaNO₂ = 0

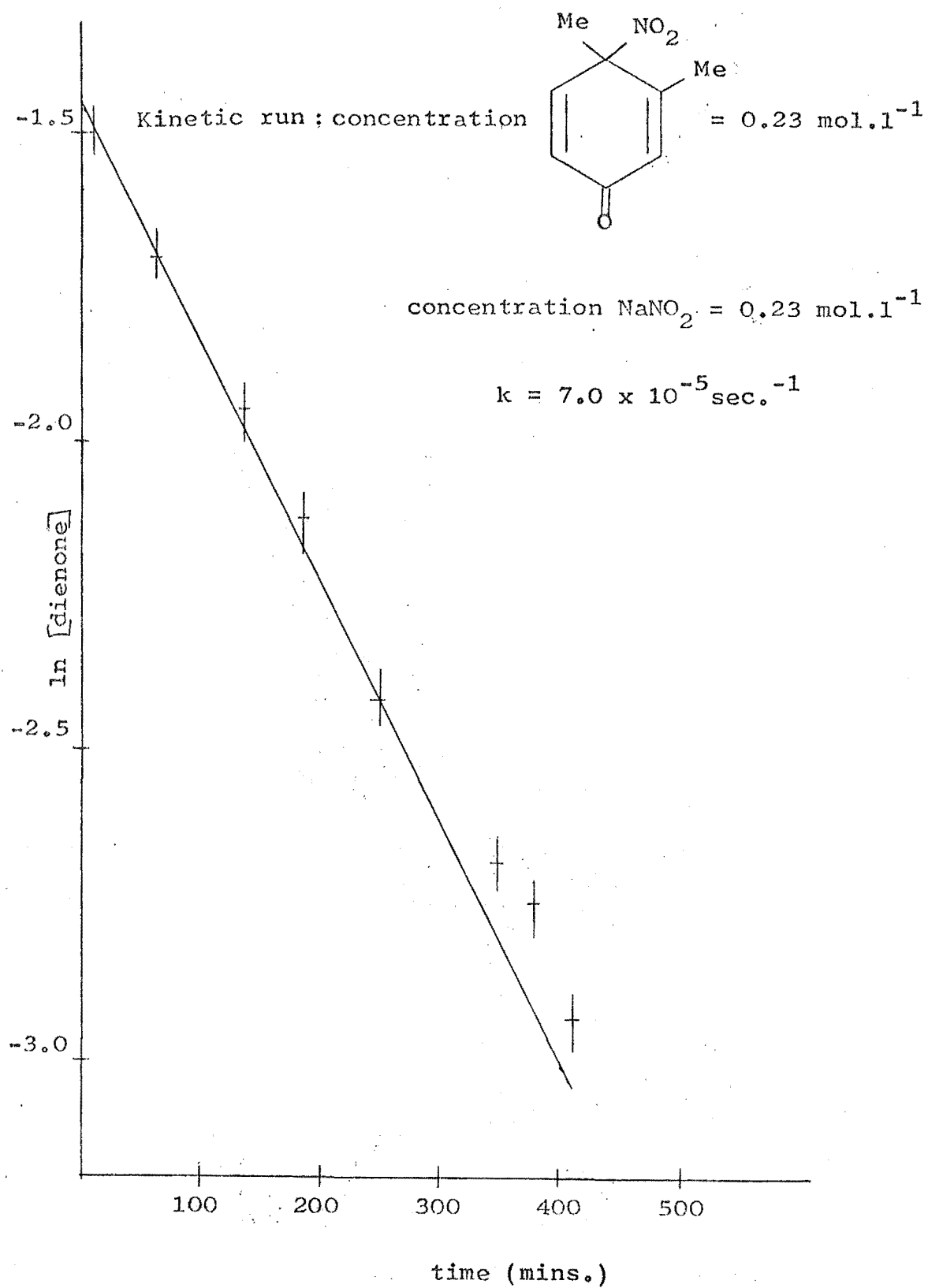
$$k = 3.6 \times 10^{-6} \text{ sec.}^{-1}$$

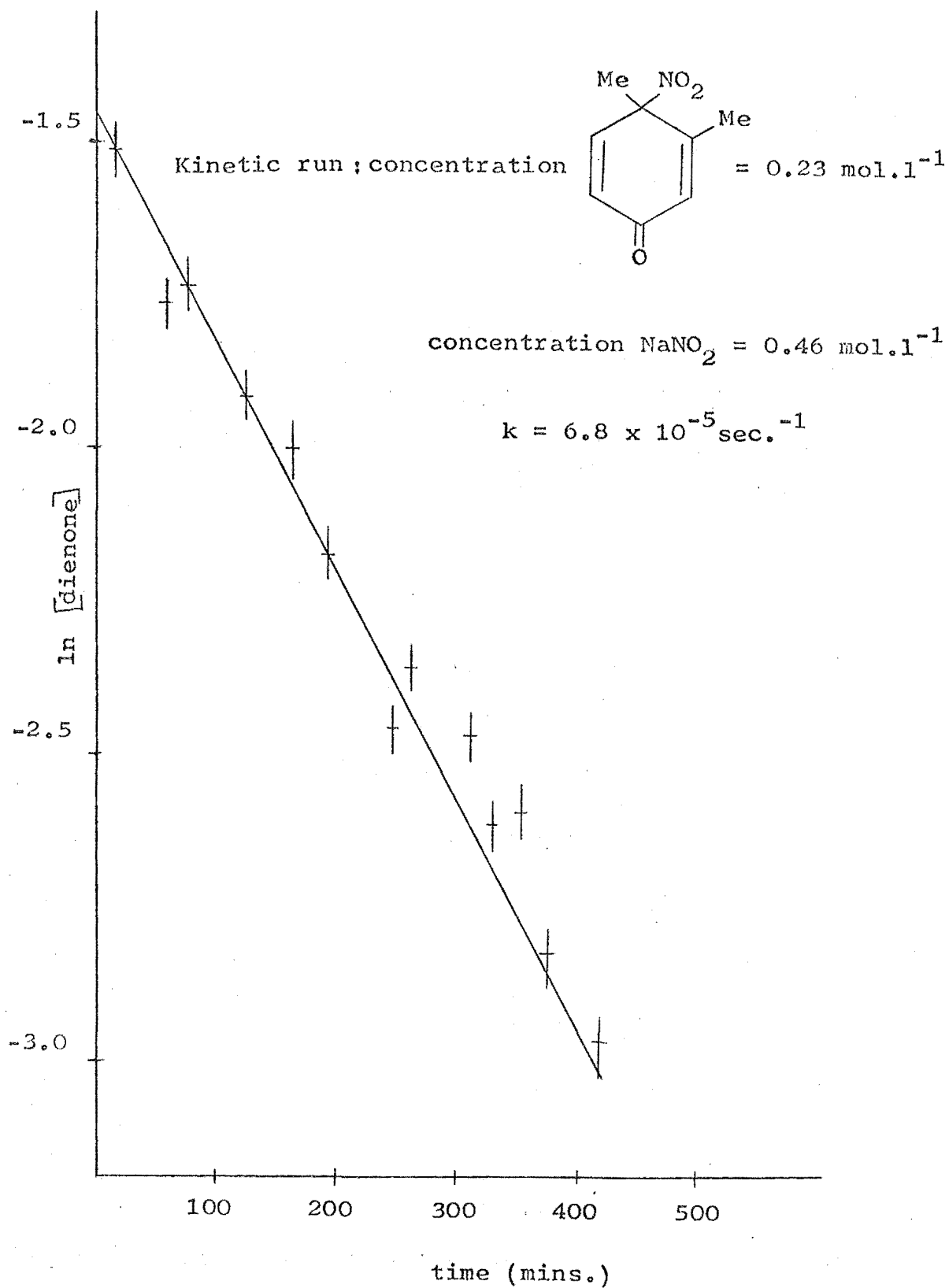












concentration due to reaction. The graphs show the first order rate constant for the trimethyldienone rearomatisation is $3.7 \pm 0.4 \times 10^{-6} \text{ sec.}^{-1}$ while the corresponding value for the dimethyldienone rearomatisation is $7.0 \pm 0.8 \times 10^{-5} \text{ sec.}^{-1}$. The addition of sodium nitrite made no difference to the rate of reaction.

Table XVIII

First order rate constants for the rearomatisation of 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one

[dienone] mol.l ⁻¹	[NaNO ₂] mol.l ⁻¹	k ₁ x 10 ⁶ sec. ⁻¹
0.11	0	3.6
0.22	0	4.0
0.22	0.22	3.9
0.22	0.44	3.7

Table XIX

First order rate constants for the rearomatisation of 3,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-one

[dienone] mol.l ⁻¹	[NaNO ₂] mol.l ⁻¹	k ₁ x 10 ⁵ sec. ⁻¹
0.23	0	7.1
0.23	0.23	7.0
0.23	0.46	6.8

Overall, the rearrangements were not significantly catalysed by the addition of perchloric acid, although in the initial stages, those rearrangements run in the presence of perchloric acid underwent rearomatisation much more rapidly than those rearrangements run without acid present. (Table XX) A rearrangement run in the presence of sodium perchlorate underwent rearomatisation at the same rate as a non-acidic rearrangement throughout showing that the perchlorate ion does not have any significant salt effect.

Table XX

Rearomatisation of the dimethyldienone in the presence of perchloric acid		Rearomatisation of the dimethyldienone without the presence of perchloric acid	
Time (mins)	dienone (mol.l ⁻¹)	Time (mins)	dienone (mol.l ⁻¹)
0	0.24	0	0.24
15	0.20	13	0.22
34	0.17	38	0.18
42	0.17	40	0.19
57	0.16	60	0.17
90	0.14	92	0.15
170	0.11	170	0.13
330	0.04	330	0.06

Dienone rearrangements: summary of results

3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one

- (i) rearomatisation is first order in dienone with
 $k_1 = 3.7 \pm 0.4 \times 10^{-6} \text{ sec.}^{-1}$
- (ii) N^{15}/N^{14} ratio = 0.18 for rearomatisations run
 with equimolar concentrations of dienone and
 sodium nitrite
- (iii) halving the amount of available N^{15} enriched
 sodium nitrite halved the N^{15}/N^{14} ratio
- (iv) doubling the concentration of N^{15} enriched
 sodium nitrite increased but did not double
 the N^{15}/N^{14} ratio
- (v) the rate of rearomatisation was not affected
 by any of the changes in (iii) or (iv)
- (vi) overall, the reaction was not significantly
 acid catalysed by perchloric acid.

3,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-one

- (i) rearomatisation is first order in dienone with
 $k_1 = 7.0 \pm 0.8 \times 10^{-5} \text{ sec.}^{-1}$
- (ii) N^{15}/N^{14} ratio = 0.42 for rearomatisations run
 with equimolar concentrations of dienone and
 sodium nitrite
- (iii), (iv), (v) and (vi) as for 3,4,5-trimethyl-4-
 nitrocyclohexa-2,5-dien-1-one.

D I S C U S S I O N

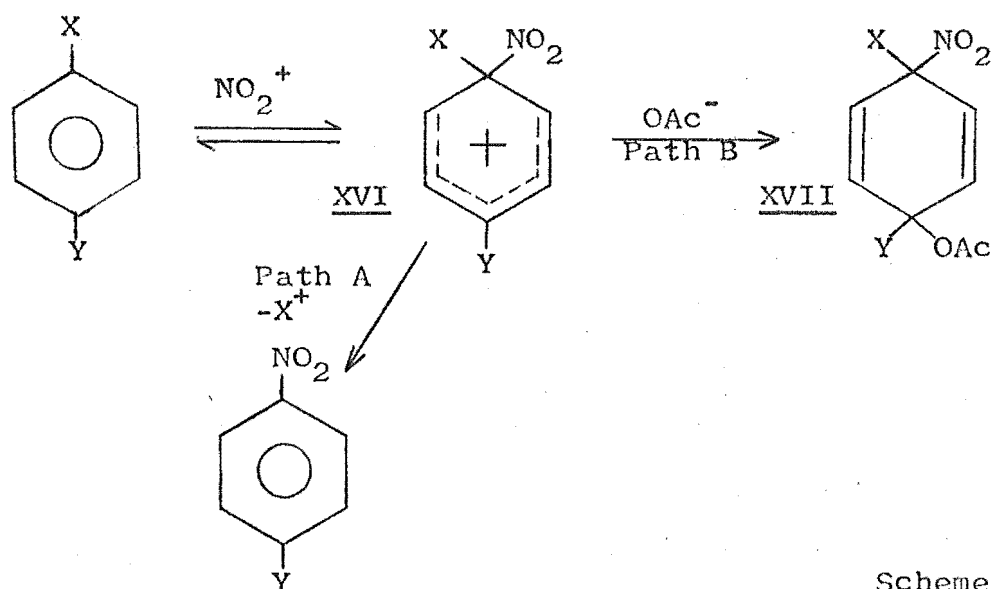
This discussion covers various aspects of the reaction of aromatic substrates with nitric acid-acetic anhydride mixtures. The first section deals with the evidence for ipso-nitration at ring positions bearing substituents other than the methyl group. A summary of the formation mechanisms of those nitration products once considered anomalous, e.g.: aryl acetates and side-chain nitro products, obtained from the nitration of various polymethylbenzenes in nitric acid-acetic anhydride presents the evidence for believing that these products arise from ipso-nitration at a methyl-substituted ring position. Using this as a basis, it is then possible to explain the similar types of product found in this work in terms of ipso-nitration at ring carbons bearing substituents other than the methyl group. The second section deals with the product distributions obtained from the nitrations of the various compounds studied in this work and the kinetic competition nitrations between some of these compounds. The third section discusses the rearomatisation mechanism of the nitrocyclohexadienones formed.

The formation of nitration products other than ring nitro products

There are many possible reaction paths that may be followed after the initial ipso-nitration at an X-substituted ring position has occurred. These are

The best evidence for ipso-nitration at the X-substituted ring position is the isolation of the dienes (XVII) or dienones (XX) in which the NO_2 and X groups remain attached to the same ring carbon. In many cases in this work, however, the dienes and dienones could not be isolated and the occurrence of ipso-nitration must be deduced from the nature of the products isolated from the reactions. Scheme X indicates that the formation of aryl acetates (XXII), side-chain products (XIX), nitrophenols (XXI) as well as dienes and dienones, all have nitration at the X-substituted ring position as the first step. Isolation of such products (ipso-products) may, therefore, be taken as evidence of ipso-nitration. Scheme X is best discussed by considering each of the possible pathways separately.

(i) Loss of X and diene formation

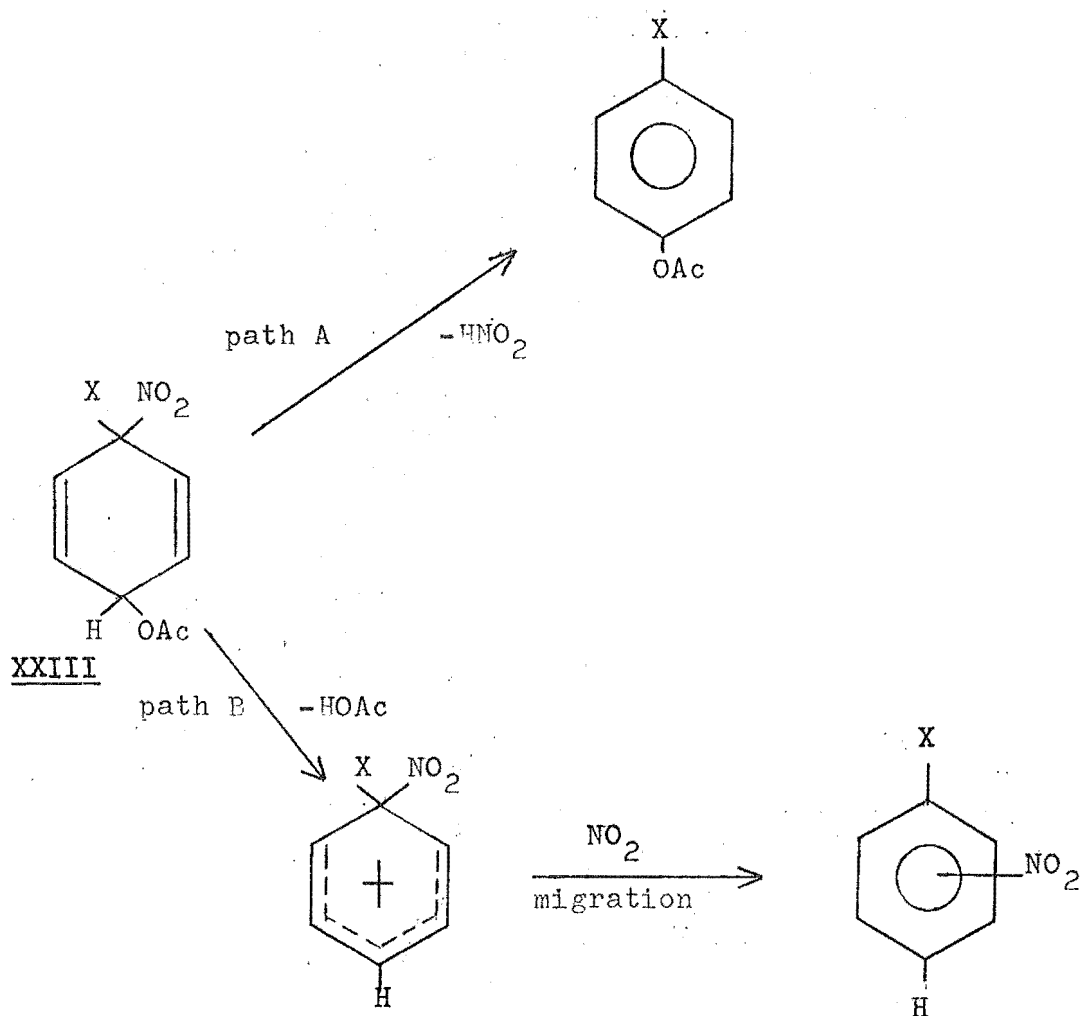


Scheme (XI)

Once a benzenonium ion (XVI) is formed as a result of ipso-nitration at the X-substituted ring position, one of the many possible reaction paths is the loss of X as X^+ (path A). This is especially favourable if X is a tertiary or even secondary alkyl group. Olah and Kuhn⁸⁸ showed that "normal" ring nitration is accompanied by electrophilic dealkylating nitration for ortho-and para-cymene and para-di-isopropylbenzene when these compounds are nitrated with nitronium tetrafluoroborate. Hahn and Strack⁸⁹ also observed nitro-deisopropylation from para-cymene. When X^+ is a poorer leaving group than NO_2^+ , two other reaction pathways are possible; (i) the loss of NO_2^+ leading to no overall reaction and (ii) the trapping of a nucleophilic species (OAc^-) at the formally positively charged position para to the ipso site to form a diene (XVII) (path B). Only 1,4-diene adducts are obtained by this process in all of the addition reactions studied. Two reasons can be advanced for the absence of 1,2-adducts. First, the para position in the cyclohexadienyl cation has a greater positive charge than the ortho position⁹⁰ and should, therefore, be more reactive towards nucleophiles. Second, there would be severe eclipsing interactions in the 1,2-adduct between the NO_2 or methyl group and the adjacent acetate group. In most

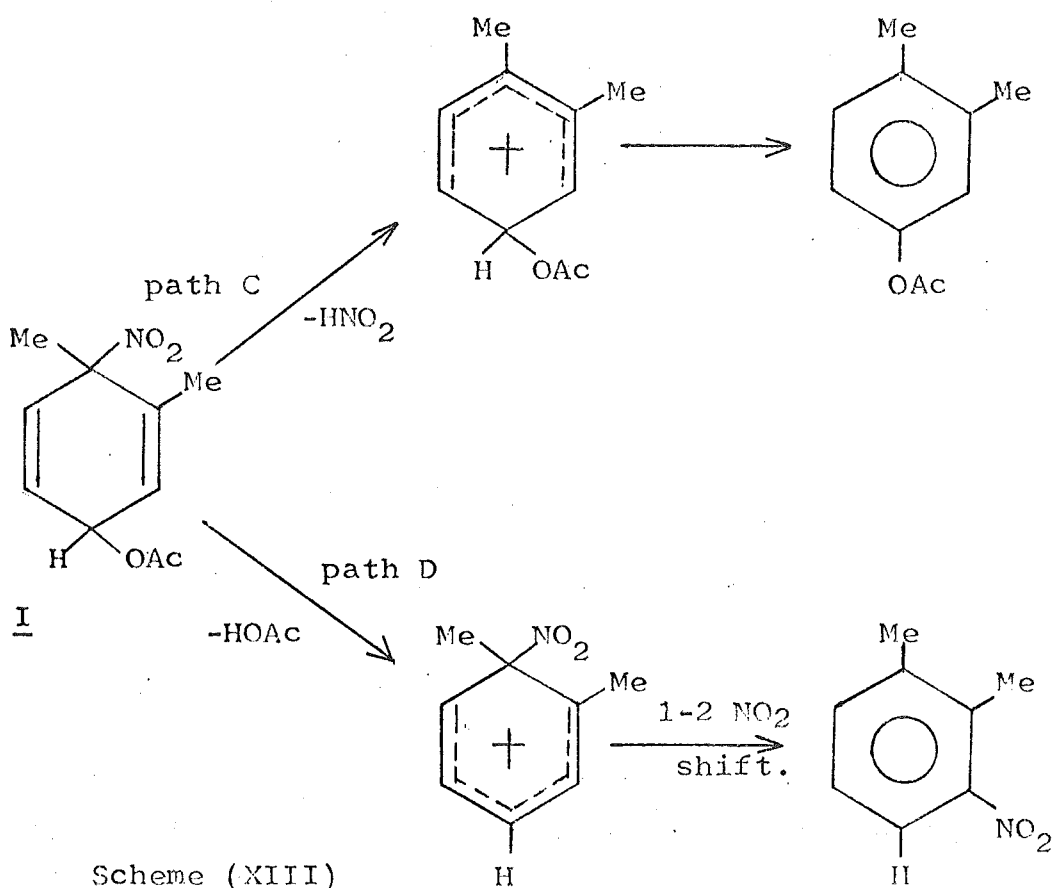
of the work done outside this thesis the group X, scheme XI, is the methyl group where path B is favoured and several diene acetate adducts are known. The diene may be a secondary acetate adduct (XVII Y = H), or a tertiary acetate adduct, (XVII Y = CH₃). These two possibilities lead to widely differing reaction products and are best discussed separately.

(ii). Reactions of a secondary acetate adduct



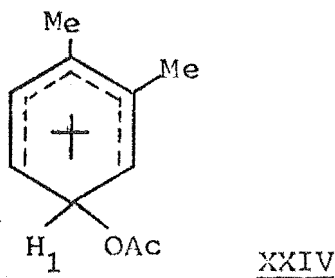
Scheme (XII)

Several examples of secondary acetate adducts (XXIII) are known^{10,11,91,92}. These dienes decomposed in one or both of two ways depending on the decomposition conditions. One way is by the loss of nitrous acid to give an aryl acetate (path A, scheme XII)^{10,11} and the other is through loss of acetic acid and a nitro group migration to give ring nitro products (path B, scheme XII). The rearomatisation of the ortho-xylene adduct (I) in a weak acetic acid solution can be taken as a typical example (scheme XIII). As the ester



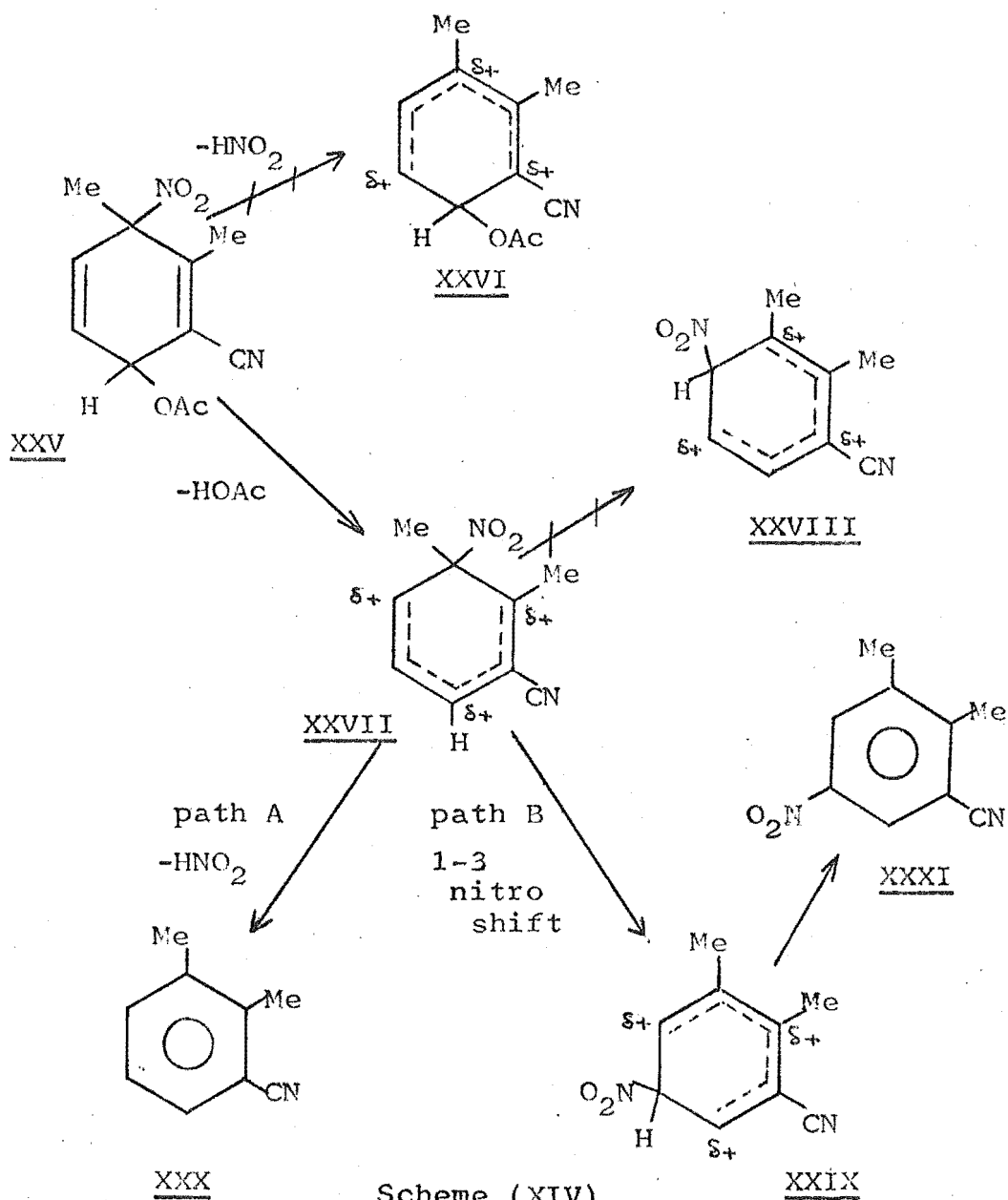
function is more basic than the nitro group, protonation of the acetate and loss of acetic acid to give 3-nitro-

o-xylene (path D, scheme XIII) might be expected to be favoured over path C, involving acid catalysed fission of the nitro group. However, decomposition of the o-xylene adduct (I) under weakly acidic conditions, gives predominantly aryl acetate. This suggests⁹³ that the nitro group is not lost in an acid-catalysed unimolecular fission but in a bimolecular process in which the geminal (H-1) proton is removed concurrently by a basic species. As only weak bases are present, e.g. acetic acid, removal of the 1-H proton is not expected to be far advanced at the transition state; i.e. the transition state will be near the classical phenonium ion (XXIV). Presumably it is this assistance provided by the removal of the 1-H proton concurrent



with the loss of the nitro group which makes the elimination to the aryl acetate preferred under weakly acidic conditions. When the rearomatisation is done in sulphuric acid medium, the basicity is very low and this assistance is lost to a large extent. Consequently, pathway D is then preferred; the diene loses acetic acid and undergoes a 1-2 or 1-3 nitro shift to give an aromatic nitro product.

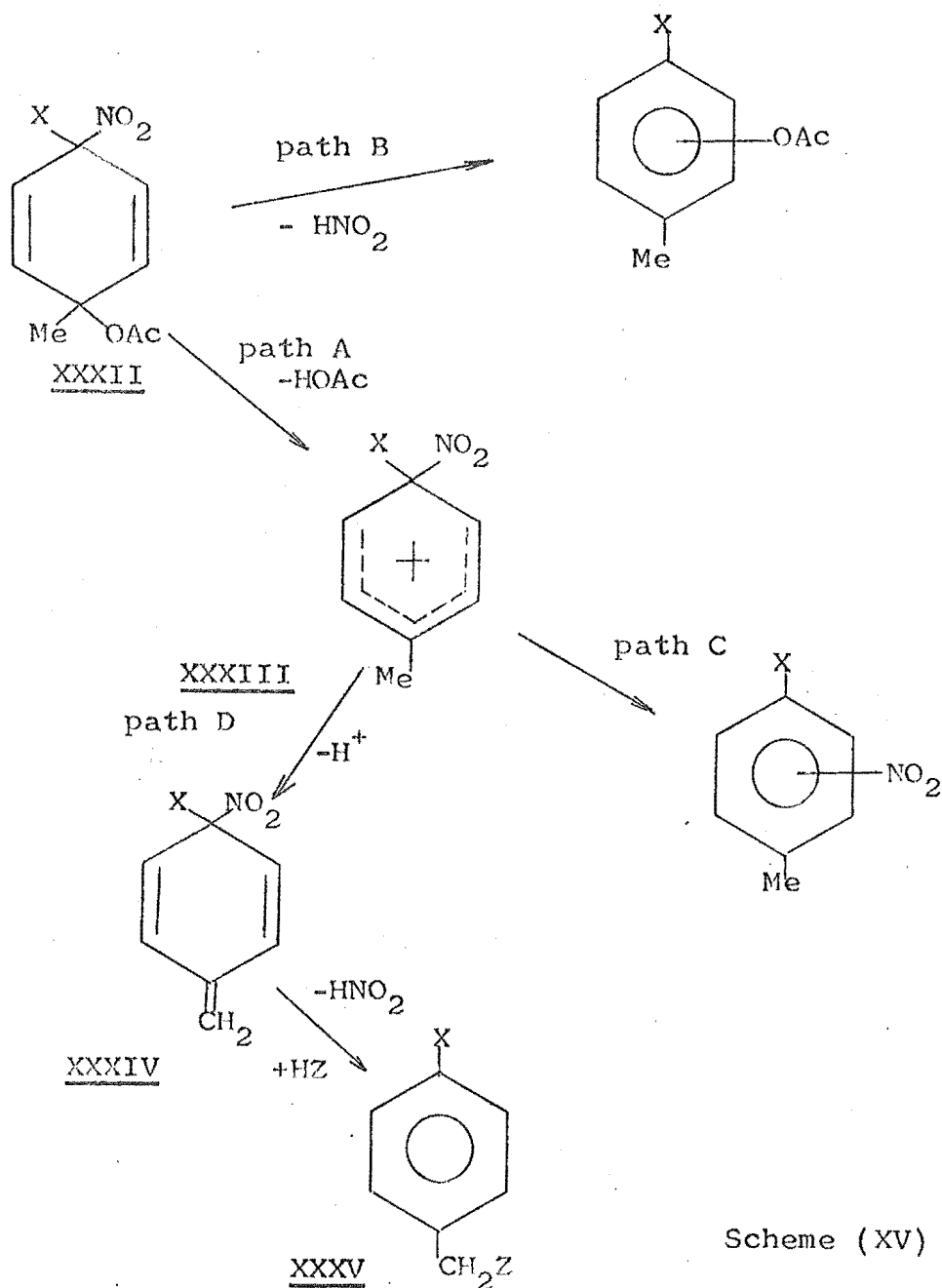
In the case of (I) at least, the nitro group is believed to undergo a 1-2 shift⁹⁴ because only 3-nitro-o-xylene is formed when rearomatisation is carried out via path D using 70% aqueous sulphuric acid. In other circumstances, the nitro group is known to undergo a 1-3 shift. A clear example of this is found in the rearomatisation of the diene adduct (XXV, scheme XIV).



The major rearomatisation products obtained on heating (XXV) in inert solvent or acetic acid are 2,3-dimethylbenzonitrile (XXX) and its 5-nitro derivative (XXXI). The initial step in the rearrangement is loss of the acetate group because loss of the nitro group leads to the ion (XXVI) in which the nitrile substituent is attached to a ring carbon carrying a formal positive charge. Loss of the acetate leads to the more stable ion (XXVII) where the charge on the ring carbon bearing the nitrile group is formally zero. The transition state leading to (XXVII) is therefore expected to be of lower energy than that leading to (XXVI). The ion (XXVII) can either lose a nitro group to give 2,3-dimethylbenzonitrile (path A, scheme XIV) or undergo a 1-3 nitro shift to give (XXIX) (path B, scheme XIV). A 1-2 nitro shift results in the carbon atom to which the nitrile group is attached acquiring a formal positive charge (XXVIII). This is energetically unfavoured compared to the 1-3 shift which maintains the zero charge on this carbon atom. The 1-3 shift is apparently intramolecular because the amount of (XXXI) formed is not decreased when the rearomatisation is carried out in the presence of reactive arenes such as mesitylene.

(iii) Reactions of a tertiary acetate adduct

A few tertiary acetate adducts have been isolated^{11,20}. The simple 1,4 elimination of nitrous acid cannot occur



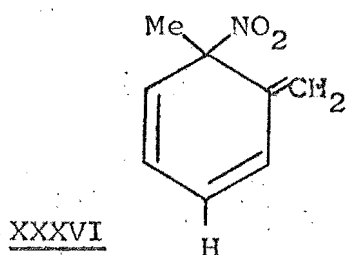
Scheme (XV)

for tertiary adducts and they exhibit a wider range of rearomatisation reactions than the secondary adducts. However, as for the secondary adducts, the first step in the rearomatisation involves either loss of nitro group (path B, scheme XV) or loss of acetate (path A).

If the adduct loses acetate, the benzenonium ion (XXXIII) is generated. The ion (XXXIII) reacts either by a nitro shift to give a nitroarene (path C) or by the abstraction of a proton from the para-methyl group to give an exocyclic diene (XXXIV) leading to side-chain products (XXXV) (path D). The group Z in the side-chain products (XXXV) arises from the nucleophilic species HZ in which the rearomatisation is run; e.g. Z=OMe in methanol, OAc in acetic anhydride-acetic acid. Exocyclic dienes (XXXIV) are believed to be key intermediates in the formation of side-chain products,^{14,19,20} although there is no direct evidence for their existence. None have been isolated or detected during the course of nitration reactions carried out at $-60^{\circ}20$. Nevertheless, the mechanism drawn out in scheme XV, in which formation of the exocyclic diene (XXXIV) plays a prominent role, allows a rational explanation of the range of products formed by the rearomatisation of tertiary acetate adducts under different rearomatisation conditions. A well studied adduct is that from p-xylene (scheme XV, $X=CH_3$).⁹⁵ The result of the competition between pathways C and D is found to depend on the strength and concentration of the bases present in the rearomatisation medium. The stronger the base and the higher its concentration the more likely it is that deprotonation of (XXXIII, path D) will occur before the nitro shift (path C). When the rearomatisation of the p-xylene adduct is carried out in the presence

of sulphuric acid or nitric acid, the strongest bases available to deprotonate (XXXIII) are the liberated acetic acid and nitrous acid and their concentrations are low. Consequently, path C is favoured over path D and the major rearomatisation product is 2-nitro-p-xylene. On the other hand, when decomposition is carried out in methanol, this more basic solvent, present in high concentration, efficiently deprotonates (XXXIII) and no 2-nitro-p-xylene is formed; the product is (XXXV, Z=OMe).

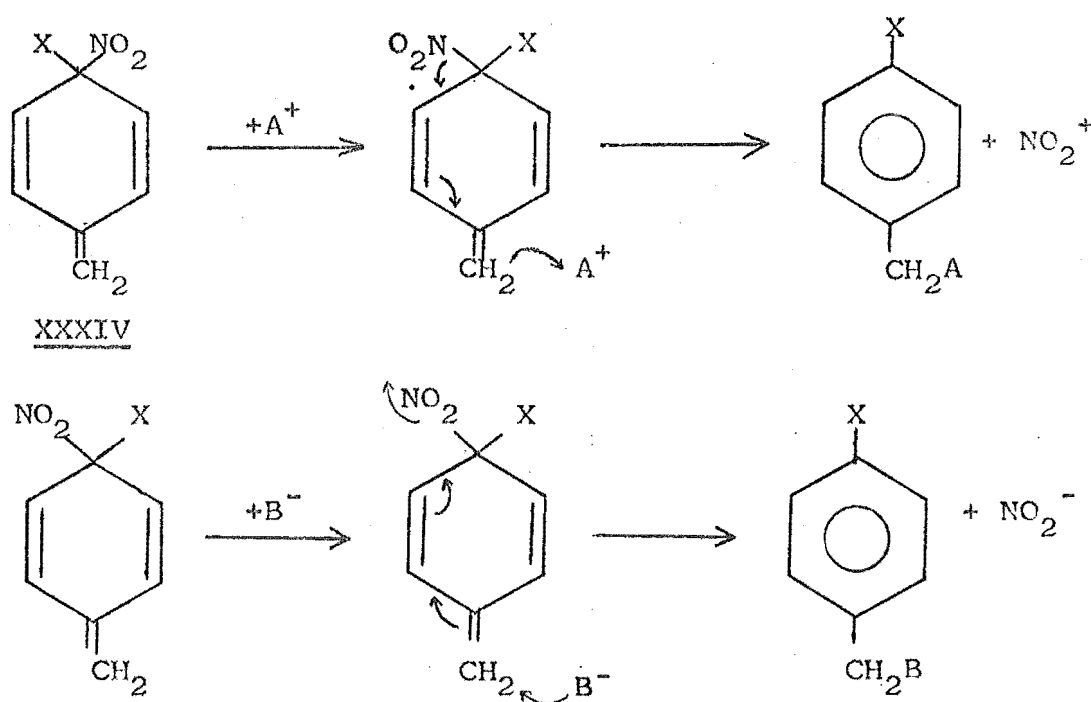
It has been established from a study on nitration of certain polymethylbenzenes¹⁴ that the proposed exocyclic diene intermediates must have a cross-conjugated triene structure (e.g. XXXIV) and not a conjugated triene structure (e.g. XXXVI). Firstly, only those methyl-



benzenes with methyl groups para to each other form side-chain derivatives; secondly, the side-chain derivatives formed are those in which the substituted methyl group is para to the most activated ipso position; thirdly, only those adducts which have a methyl group ipso to the acetate give side-chain products - secondary acetates do not - and fourthly,

the methyl group substituted is ipso to the acetate and para to the position of nitronium ion attack, not at positions ortho or ipso to the initial electrophilic attack.

Once the exocyclic diene (XXXIV) has formed there are two possible mechanisms by which it may rearrange to the side-chain product. The first mechanism (A) is



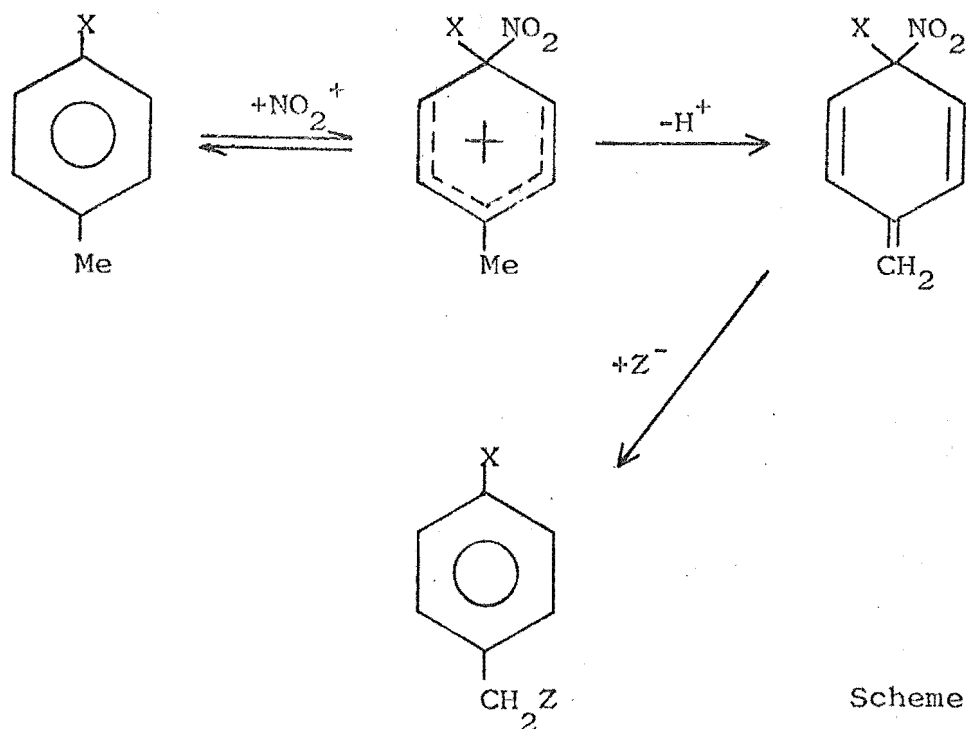
Scheme (XVI)

considered unlikely⁹⁵ because attempts to detect the release of nitronium ion from the cyclohexadienyl cation formed from hexamethylbenzene by trapping with mesitylene⁹⁶ were unsuccessful and the nitronium ion is expected to be a better leaving group from a positively charged cyclohexadienyl cation than an uncharged exocyclic diene.

In addition, the side-chain nitro derivative often forms in competition with side-chain esters which can only arise directly from nucleophilic attack. It seems unlikely that both side-chain nitro and side-chain ester compounds would form at comparable rates under quite different conditions as observed,⁹⁵ if they were formed by different mechanisms. It is probable, therefore, that all side-chain products arise from nucleophilic attack on the exocyclic diene (XXXIV); by nitrous acid to give side-chain nitro products, by acetic acid to give benzylacetates or by methanol to give benzylmethylether. Nitrous acid and acetic acid are liberated from the adducts during rearomatisation and are available to compete as nucleophiles against any introduced nucleophiles.

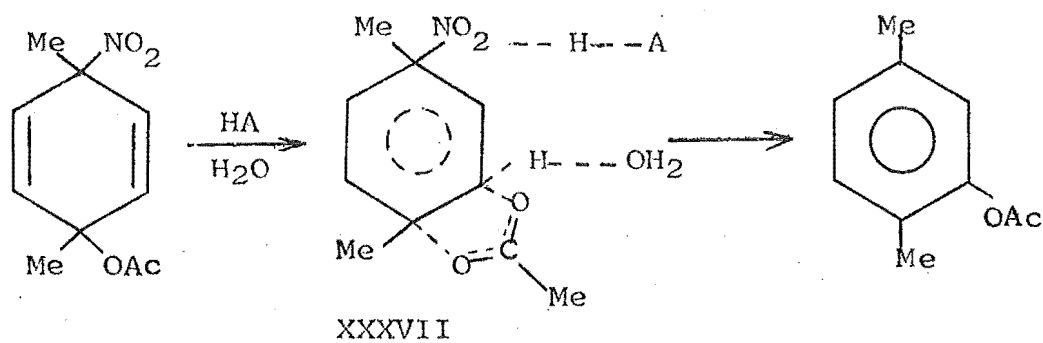
Although tertiary acetate adducts have been shown to rearrange to give side-chain products,²⁰ it is not certain whether these adducts are necessary intermediates in the formation of the side-chain products or not. The other possible mechanism by which the side-chain products may be formed is shown in scheme XVII in which the benzenonium ion resulting from ipso-nitration goes directly to the exocyclic diene. However, whichever mechanism (scheme XV, path D) or (scheme XVII) is correct, the first step in the formation of side-chain products is ipso-nitration at the ring position para to the side-chain. Thus formation of side-chain products is evi-

dence for ipso-nitration.



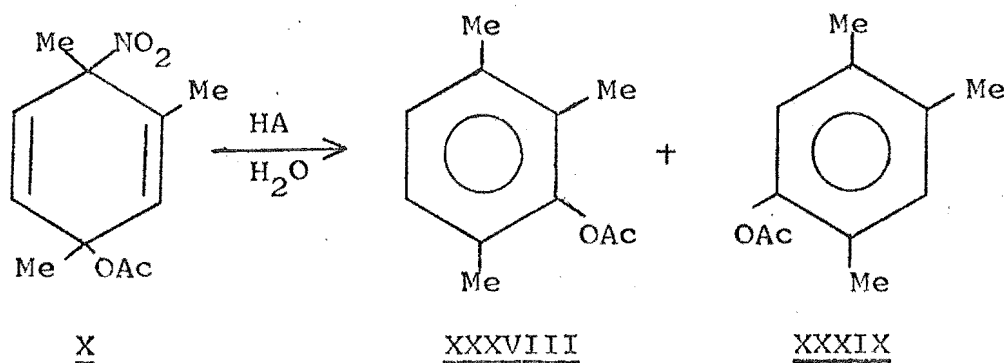
Tertiary acetate adducts may also rearrange by path B (scheme XV) to give aryl acetates. The *p*-xylene adduct has been studied in some detail.⁹⁵ Pathway B is most favoured when the diene rearomatisation is carried out in wet acetic acid. Water catalyses the reaction and has a profound effect on the rearrangement mechanism. Rearomatisation of the *p*-xylene adduct in wet acetic acid goes to completion in thirty minutes and gives acetoxy-*p*-xylene as the only product, whereas in anhydrous acetic acid the reaction takes eighteen hours and gives a mixture of products arising from both pathways A and B (scheme XV). This suggests that the re-

arrangement mechanism may be a concerted acid-catalysed loss of nitro group accompanied by acetate migration with water acting as a base to remove the proton in the transition state (XXXVII). Support for the 1-2 acetate



Scheme (XVIII)

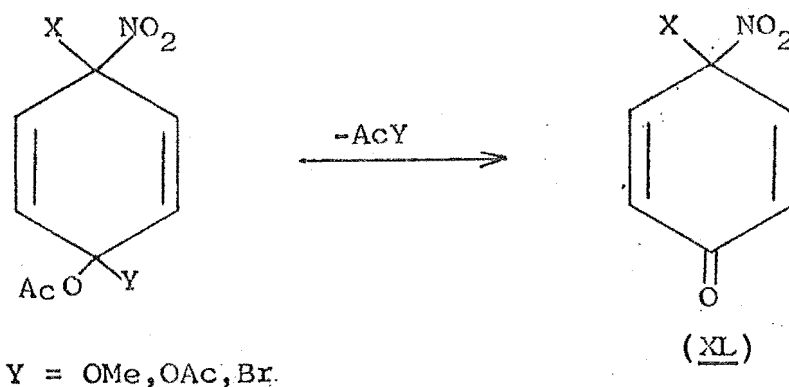
shift comes from a study of the diene (X)¹⁹ which, on rearrangement in aqueous acid, gives (XXXVIII) and (XXXIX) as major products.



(iv) Dienes with Br, OAc or OMe groups ipso to the acetate

Only one of these unstable dienes has been character-

ised.⁹⁷ Such dienes decompose to give a nitrocyclohexa-2,5-dien-1-one (XL) and several of these compounds have



been isolated.^{13,98} The dienones ultimately rearrange to nitrophenols.

The most important point to emerge from these studies on the formation of "anomalous" nitration products in acetic anhydride-nitric acid is that they all result from the initial ipso-nitration at a methyl-substituted ring position. Consequently, isolation of side-chain nitro products and aryl acetates as well as dienes and dienones is evidence for ipso-nitration.

The evidence provided by this thesis for ipso-nitration at aromatic ring carbon atoms bearing substituents other than methyl groups

It has been found in this work that ipso-nitration will occur at ring carbons bearing ethyl or methoxy groups and bromine or chlorine atoms. Table XXI presents

the evidence for this. The nitration products are categorised as arising either from ipso-nitration or normal nitration, i.e. nitration at an unsubstituted ring position, and the amount of each product is given as a percentage of the total yield.

Table XXI

Compound nitrated: para-diethylbenzene

<u>Product</u>	<u>Origin</u>	<u>%</u>
4-(α -nitroethyl)-ethylbenzene	<u>ipso</u> -nitration at an ethyl-substituted ring position	55
1,4-diethyl-1-acetoxy-4-nitrocyclohexa-2,5-diene	<u>ipso</u> -nitration at Et	10
2-nitro-1,4-diethylbenzene	normal nitration	35

Compound nitrated: para-ethyltoluene

<u>Product</u>	<u>Origin</u>	<u>%</u>
4-(α -nitroethyl)-toluene	<u>ipso</u> -nitration at Me	35
4-ethyl-phenylnitromethane	<u>ipso</u> -nitration at Et	30
2-nitro-4-ethyltoluene	normal nitration	18
3-nitro-4-ethyltoluene	normal nitration	14
2-acetoxy-4-(α -nitroethyl)-toluene	<u>ipso</u> -nitration at Me	2
3-acetoxy-4-ethyltoluene	<u>ipso</u> -nitration at Me	1

..../Cont. page 83

Compound nitrated: ethylmesitylene

<u>Product</u>	<u>Origin</u>	<u>%</u>
3,5-dimethyl-4-ethyl-phenyl-nitromethane	<u>ipso</u> -nitration at Et	>98
nitroethylmesitylene	normal nitration	< 2

Compound nitrated: bromomesitylene

<u>Product</u>	<u>Origin</u>	<u>%</u>
2,4-dibromo-6-nitro-mesitylene	uncertain	45
nitromesitylene	<u>ipso</u> -nitration at Br	41
nitrobromomesitylene	uncertain	14

Compound nitrated: 2,4,6-trimethoxybromobenzene

<u>Product</u>	<u>Origin</u>	<u>%</u>
2,4,6-trimethoxynitro-benzene	<u>ipso</u> -nitration at Br	48
1,3-dibromo-5-nitro-2,4,6-trimethoxybenzene	uncertain	22
nitro-2,4,6-trimethoxy-bromobenzene	uncertain	20
1,3,5-tribromo-2,4,6-trimethoxybenzene	uncertain	10

Compound nitrated: chloromesitylene

<u>Product</u>	<u>Origin</u>	<u>%</u>
nitrochloromesitylene	normal nitration	78
3,5-dimethyl-4-chloro-phenylnitromethane	<u>ipso</u> -nitration at Cl	20
dinitrochloromesitylene	normal nitration	2

.... /Cont. page 84

Compound nitrated: 2,4,6-trimethoxychlorobenzene

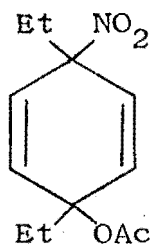
<u>Product</u>	<u>Origin</u>	<u>%</u>
3-nitro-2,4,6-trimethoxy-chlorobenzene	normal nitration	75
3,5-dimethoxy-4-chloro-4-nitrocyclohexa-2,5-dien-1-one	<u>ipso</u> -nitration at Cl	25

Compound nitrated: methoxymesitylene

<u>Product</u>	<u>Origin</u>	<u>%</u>
3,5-dimethyl-4-methoxy-phenylnitromethane	<u>ipso</u> -nitration at OMe	60
2,4,6-trimethyl-4-nitro-cyclohexa-2,5-dien-1-one	<u>ipso</u> -nitration at Me	29
2-acetoxy-3,5-dimethyl-4-methoxyphenylnitromethane	uncertain	11

(i) Ipso-nitration at ring carbons bearing ethyl groups

The isolation of one of the stereo-isomers of the diene (XLI) is direct proof of ipso-nitration at the



XLI

ethyl-substituted ring position in para-diethylbenzene.

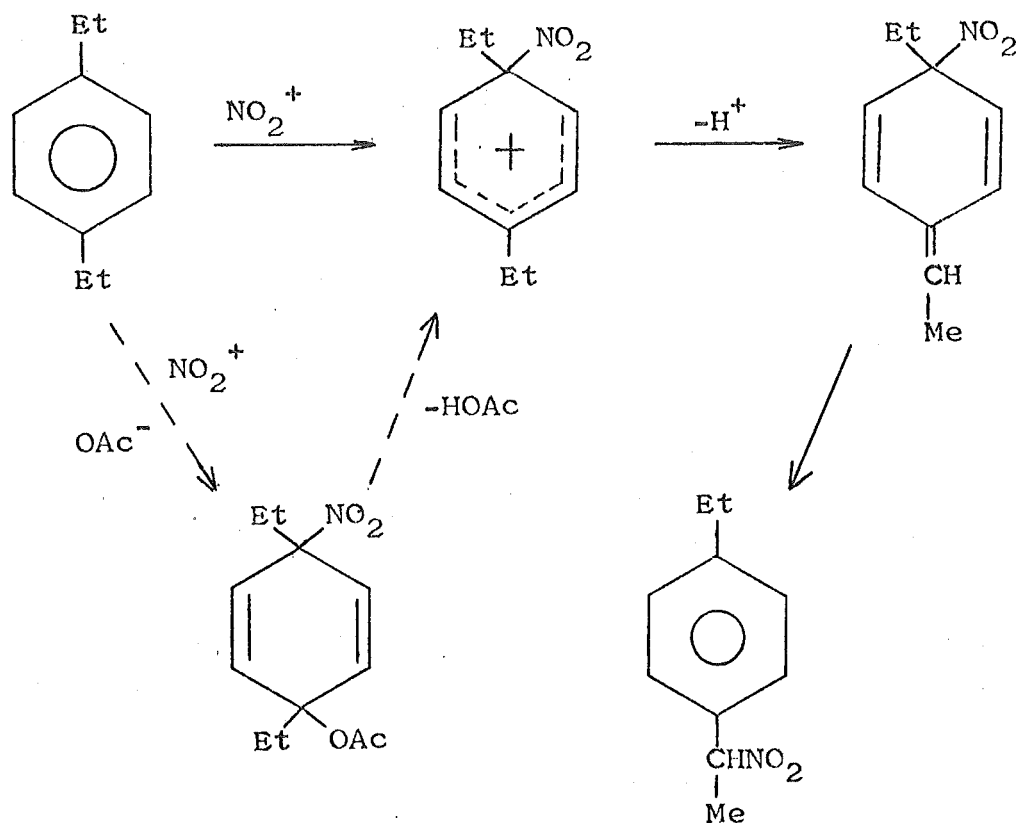
It is likely that the isolated isomer has the cis structure on the basis of n.m.r. evidence and comparison with the para-xylene adducts. In the case of para-xylene, the cis structure was tentatively assigned to the isomer with a proton resonance at $\delta = 6.21$ and the

trans structure to the isomer with a signal at $\delta = 6.03$.⁹⁹

The analogous proton resonance of the diene isomer isolated in this work appears at $\delta = 6.10$. Before work-up, the n.m.r. spectrum gave evidence for the presence of the other isomer. The spectrum consisted of a small singlet at $\delta = 5.95$ with a larger singlet at $\delta = 6.13$. The latter presumably belonged to the isomer eventually isolated as the signal at 5.95 disappeared quickly on heating a small sample of product mixture. Therefore, the more stable isomer has a proton resonance in the diene region $\delta = 0.18$ downfield from the more reactive isomer. The same situation arises for the para-xylene adducts and by analogy with them, the isomer obtained in this work probably has the cis structure. However, this assignment is not certain because all attempts to date have failed to positively distinguish between the cis and trans para-xylene adducts.⁹⁵

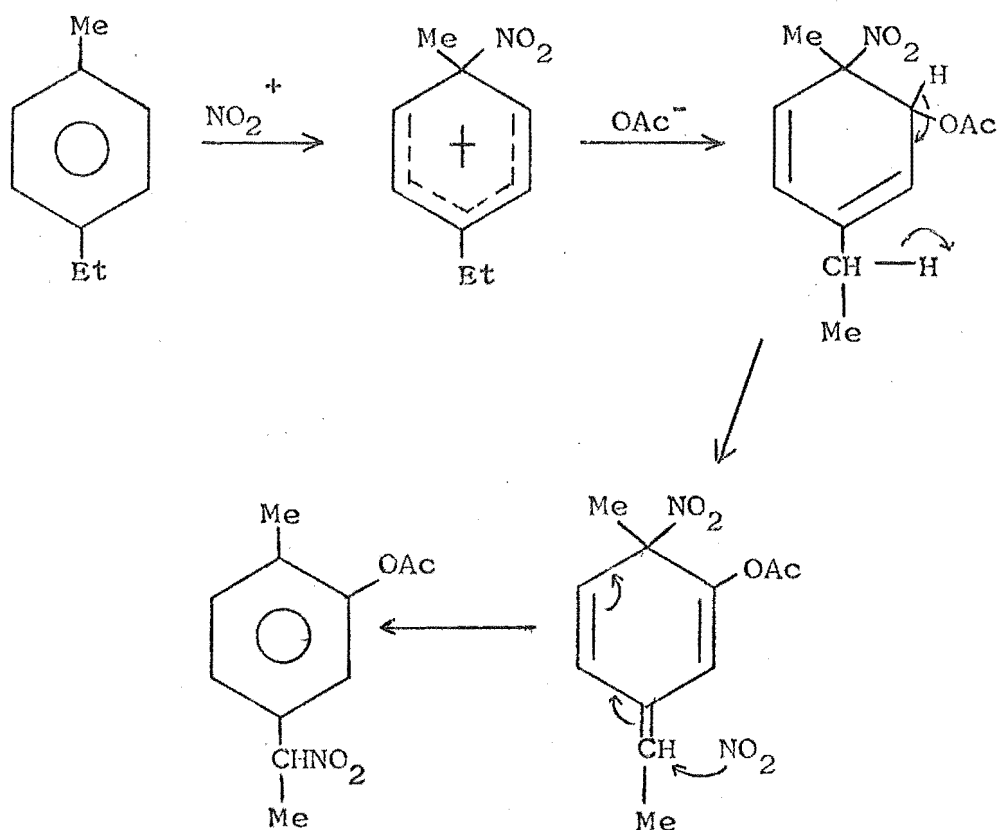
Isolation of side-chain nitro products from the nitration of para-diethylbenzene, para-ethyltoluene and ethylmesitylene is further evidence for ipso-nitration at an ethyl-substituted ring position. These products form in an analogous way (scheme XX) to the side-chain nitro products isolated from the previously discussed (pages 65 - 81) nitrations of the methylbenzenes.

The mode of formation of 2-acetoxy-4-(α -nitroethyl)-toluene, isolated from the nitration of para-ethyltoluene, is less obvious although the position of the side-chain



Scheme (XX)

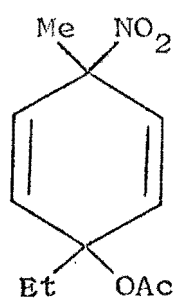
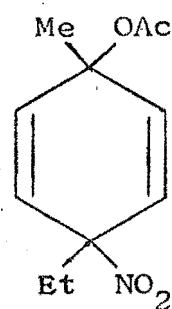
para to the methyl group, indicates that it involves ipso-nitration at the methyl-substituted ring position at some stage. This product does not arise from nitration of 3-acetoxy-4-ethyltoluene which, when reacted under the conditions used for para-ethyltoluene, gives a ring nitro product with no trace of substitution in the side-chain. Possibly, 2-acetoxy-4-(α -nitroethyl)-toluene arises via the following mechanism (scheme XXI). In this reaction sequence, 4-(α -nitroethyl)-toluene would not be formed as a discrete product. This is in agreement with experiment which shows that 2-acetoxy-4-(α -nitroethyl)-toluene does not arise by the acetoxylation



Scheme (XXI)

of 4-(α -nitroethyl)-toluene in nitric acid-acetic anhydride at 0° .

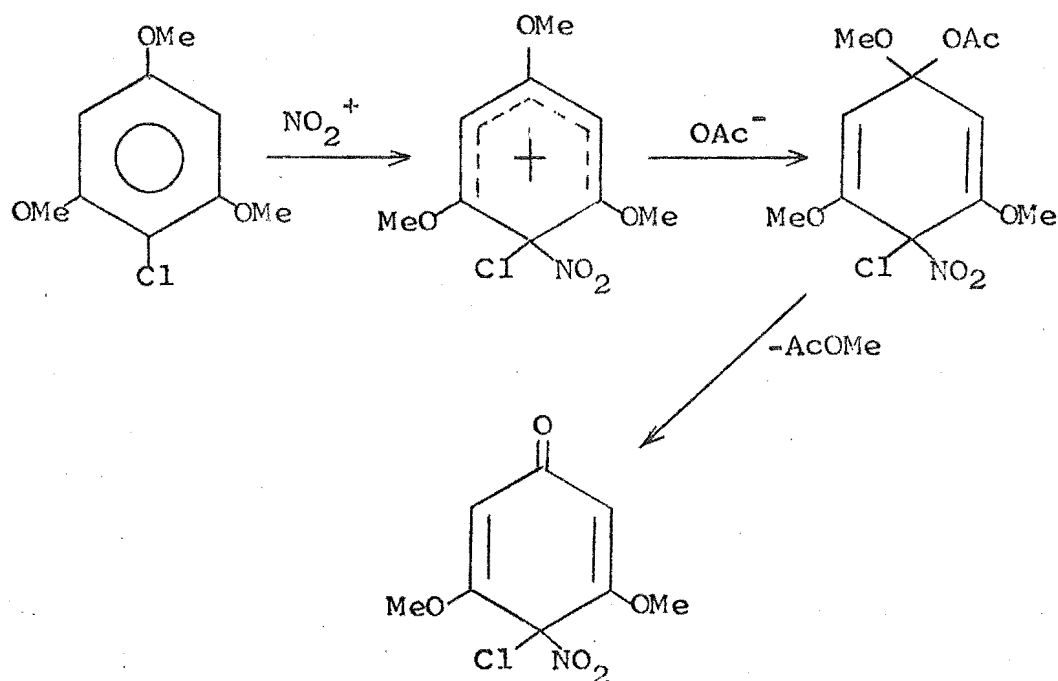
The small amount of 3-acetoxy-4-ethyltoluene isolated from the nitration of para-ethyltoluene is considered to have arisen from (XLII) by NO_2 loss and

XLIIXLIII

a 1-2 acetate shift in an analogous way to the rearrangement of tertiary acetate adducts discussed previously (p.79) rather than from (XLIII) by NO_2 loss and a 1-3 acetate shift. The isolation of 3-acetoxy-4-ethyltoluene does not, therefore, constitute evidence for ipso-nitration at the ethyl-substituted ring position.

(ii) Ipso-nitration at a ring position bearing the chloro, bromo or methoxy function

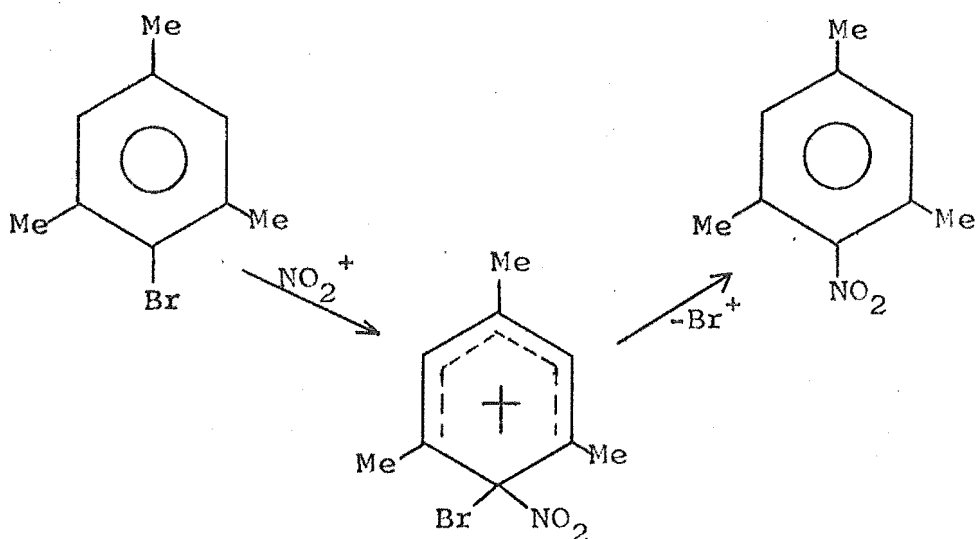
The isolation of 3,5-dimethoxy-4-chloro-4-nitrocyclohexa-2,5-dien-1-one from among the products of nitration of 2,4,6-trimethoxychlorobenzene is direct proof of ipso-nitration at a chlorine-substituted ring position. By analogy with the nitrocyclohexa-2,5-dien-1-ones formed through ipso-nitration at a methyl-substituted ring position, this product is almost certainly formed by the following reaction sequence (scheme XXII).



Scheme (XXII)

The formation of the side-chain nitro product, 3,5-dimethyl-4-chloro-phenylnitromethane during the nitration of chloromesitylene, is further evidence for nitration ipso to the chlorine-substituted ring position.

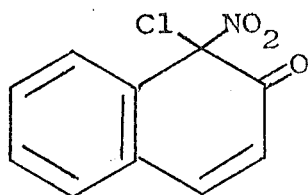
The evidence for ipso-nitration at the bromine-substituted ring position lies in the isolation of polybrominated and debrominated products from the nitration of bromomesitylene and 2,4,6-trimethoxybromobenzene. After ipso-nitration occurs at the ring position bearing the bromine substituent, the resulting benzenonium ion releases Br^+ to give, overall, a nitro-debromination reaction, e.g. scheme (XXIII).



Scheme (XXIII)

The liberated Br^+ is able to recombine with bromomesitylene to give dibromomesitylene which is not an isolated product although nitro-dibromomesitylene is. Support for this mechanism comes from a study of relative leaving abilities in electrophilic aromatic substitution.¹⁰⁰ This

shows that in acetic acid-acetic anhydride containing hydrochloric acid, 1-chloro-1-nitro-2-keto-1,2-dihydronaphthalene (XLIV) undergoes both migration and loss



XLIV

of NO_2^+ rather than Cl^+ . In contrast, the bromo analogue loses Br^+ . The conclusion is that the leaving abilities of these electrophiles increases in the order $\text{Cl}^+ < \text{NO}_2^+ < \text{Br}^+$. The same order of leaving group ability is being observed in this work. Chloromesitylene gives no evidence of Cl^+ having been released at any stage of the nitration as no polychlorinated or dechlorinated products are detected, whereas bromomesitylene shows considerable Br^+ release.

Ipso-nitration at a ring carbon bearing a methoxy group has been directly observed previously by the isolation of 3,4,5-trimethoxy-4-nitrocyclohexa-2,5-dien-1-one from the nitration products of 1,2,3,5-tetramethoxybenzene.⁹⁸ Isolation of 3,5-dimethyl-4-methoxyphenylnitromethane from the nitration of methoxymesitylene in this work provides further proof that ipso-nitration may occur at a ring carbon bearing a methoxy group.

The mode of formation of 2-acetoxy-3,5-dimethyl-4-methoxyphenylnitromethane does not appear to conform to the pattern of the other side-chain nitro products

isolated in this work although the position of the side-chain, para to the methoxy group, suggests that there has been ipso-nitration at the methoxy-substituted ring position. 2-Acetoxy-3,5-dimethyl-4-methoxyphenylnitromethane (11% of the product) does not arise either from (i) the acetoxylation of 3,5-dimethyl-4-methoxyphenylnitromethane, as treatment of this compound with acetic anhydride-nitric acid at 0° gives no reaction or (ii) the nitration of acetoxy-methoxymesitylene, because quenching the nitration reaction mixture after fifteen, thirty and sixty minutes and analysing the products (g.l.c.) gives no trace of acetoxy-methoxymesitylene as a discrete reaction product. This suggests that either the concentration of acetoxy-methoxymesitylene is too low to be detected at any stage or that the reaction pathway leading to 2-acetoxy-3,5-dimethyl-4-methoxyphenylnitromethane is different from those of other side-chain nitro products. Any attempt to draw up such a reaction pathway would, however, be totally speculative.

There is no evidence in this work for ipso-nitration at a phenyl-substituted ring position because only ring nitro products are obtained from the nitration of any of the substituted biphenyl compounds and there is no evidence to suggest these products arise by other than normal electrophilic attack at an unsubstituted ring position. Furthermore, there is no evidence for ipso-nitration at the fluorine-substituted ring position of

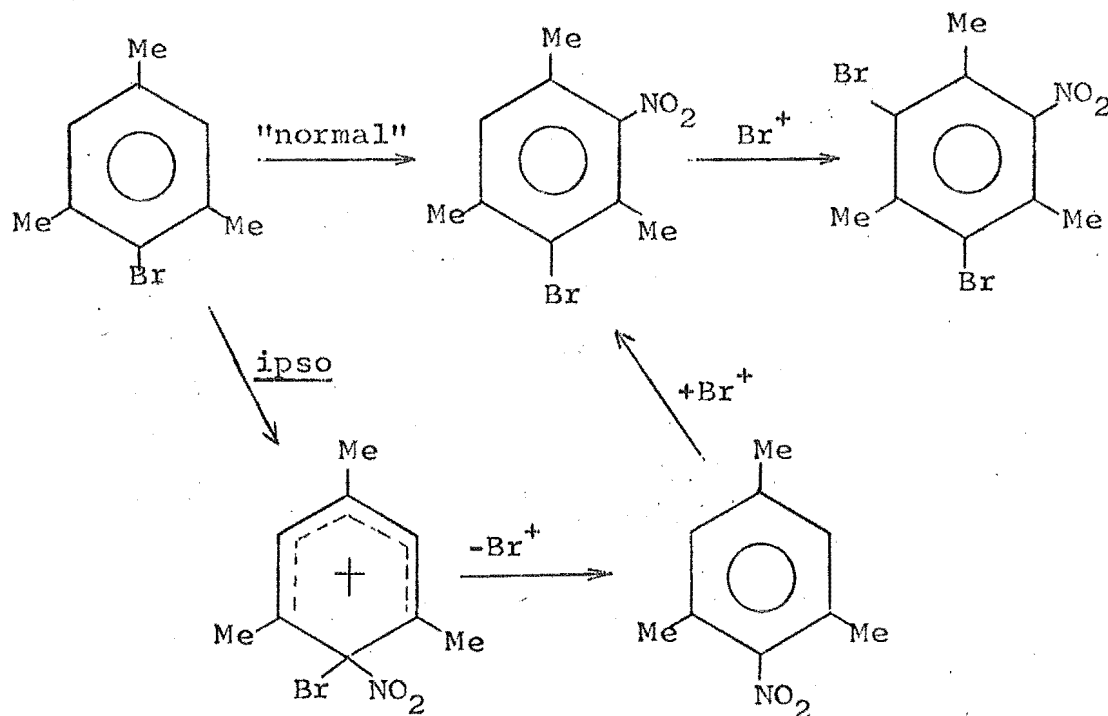
fluoromesitylene or 2,4,6-trimethoxyfluorobenzene because nitration of these compounds leads only to ring nitro products. There is nothing to suggest that these products do not arise by normal ring nitration.

Product distributions

The primary reason for performing the nitrations discussed in the previous section was to gain evidence for ipso-nitration at ring positions bearing substituents other than the methyl group. However, the product distributions obtained from these nitrations allows some insight into the factors determining the balance between ipso and non-ipso (normal) - nitration. This insight may best be gained by relating the amounts of ipso and normal nitration products observed for different compounds to the different electronic and steric requirements relevant to each instance.

The product distributions are shown in Table XXI (page 82) along with the origin of each product where known. The uncertainty associated with the formation of most of the products obtained from nitration of bromomesitylene and 2,4,6-trimethoxybromobenzene arises because there is the possibility that these products come from one or both of two reaction paths; one involving the initial ipso-nitronium ion attack at the bromine substituted ring position and the other involving normal nitration at an unsubstituted position. (Scheme XXIV)

Because of this uncertainty, it is not possible to tell the percentage of reaction products arising from ipso-nitration in these two cases.



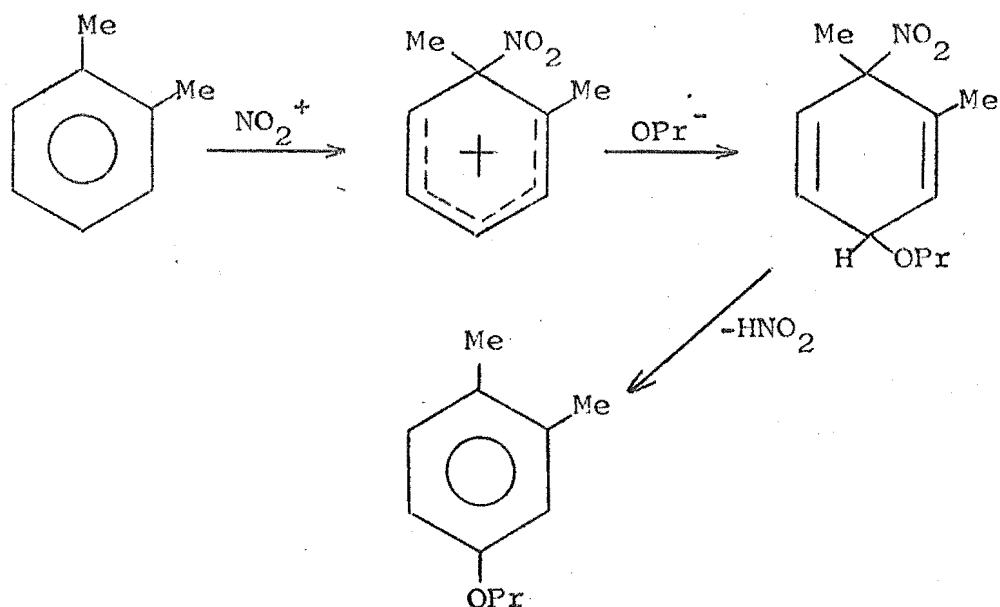
Scheme (XXIV)

In order to ensure a meaningful comparison of product distributions, certain difficulties must be taken into account. One of these concerns the possible reversibility of the initial ipso-nitration, the extent of which will vary from compound to compound. This is especially relevant for comparisons between compounds with different groups at the ipso-nitration site. The reversibility of ipso-nitration depends to some extent on the relative leaving abilities of the X^+ and NO_2^+ groups where X is the substituent at which ipso-nitration occurs. The possibility of ipso-nitration being reversible

is greatest when X^+ is a poorer leaving group than NO_2^+ . Therefore, a comparison between amounts of ipso-nitration occurring at ring positions bearing substituents of different leaving abilities, e.g. Cl^+ and Me^+ , will be less reliable than an analogous comparison between compounds bearing substituents of similar leaving abilities at the ipso-nitration site.

Another potential difficulty is that the benzenonium ion or diene adduct resulting from ipso-nitration may undergo a nitro group migration to give a normal ring nitro product. It has been shown⁹⁵ that tertiary diene adducts can rearomatise to normal ring nitro products under strongly acid conditions. However, in this thesis, when the nitration reactions that give side-chain nitro compounds as evidence for ipso-nitration are run at -46° , the n.m.r. spectra show proton resonances in the diene region. These are replaced by a single peak in the same region of the spectrum when the temperature is raised to -15° . This is interpreted as the diene adducts decomposing to give side-chain nitro products. None of the systems studied gave a detectable concurrent increase in the proton signals of the aromatic region suggesting that under the reaction conditions used, ipso-nitration does lead to recognisable ipso-products. It is also assumed that the ratio of ipso:normal nitration products mirrors the ratio of initial ipso and normal nitronium ion attack. Some support for this is provided by the product distributions obtained from the nitrations.

run using propionic anhydride-nitric acid as the nitration medium instead of acetic anhydride-nitric acid. This means that a propionate ion must now be trapped by the benzenonium ion in order that a diene adduct forms. (Scheme XX



Scheme (XXV)

Such a change, however, made no significant alteration to the final product distribution obtained from the nitration of 4-acetoxy-*o*-xylene, 5-acetoxymellitene or *o*-xylene (Table VII, page 53). This suggests that the reactions occurring subsequent to the initial nitration do not significantly affect product distributions.

Interpretation of product distributions

The product distributions obtained from an aromatic organic reaction may be rationalised either by (i) consideration of the relative reactivities of the available ring reaction sites in the ground state molecule to the

particular type of reaction in question, or (ii) consideration of relative stabilities of the transition states arising from reaction at each of the available ring sites. In the ground state approach, the reactivity of a possible reaction site depends on the π -electron density at that position as well as any steric considerations such as the presence of large groups which may block access to that reaction site. As this thesis deals with aromatic electrophilic substitution, those ring positions with the greatest π -electron density are expected to be most activated towards attack provided steric factors are not unfavourable. However, it is not possible to gain an accurate determination of electron density at the ring positions of any of the compounds studied in this thesis. The best data presently available for this purpose come from quantum mechanical calculations but these have been done only for simple molecules such as benzene and various mono-substituted benzenes. (Table XXII) Such calculations show the effects of single groups, e.g. OMe, Me, Et, C_6H_5 , F, Cl, on the π -electron distribution around a benzene ring but it is not generally considered meaningful to add these effects in order to predict the electron density at any given site in a ring substituted by two or more of these substituents. Until electron density calculations have been done for the actual compounds studied in this thesis, it is not possible to use a true ground state approach to rationalise the products obtained from any particular nitration. However, experimental quantities such as σ^+

values and partial rate factors are used to provide some estimate of the reactivity of various positions in the ground state molecule although these quantities, being experimental, are not necessarily a true measure of ground state reactivity.

Table XXII

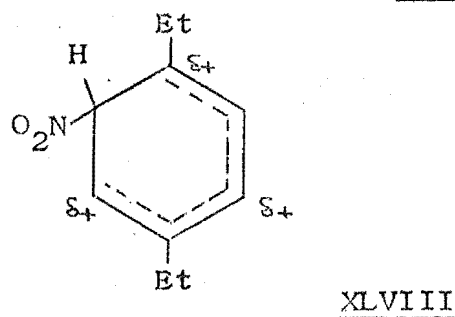
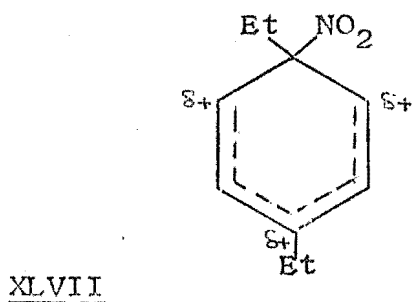
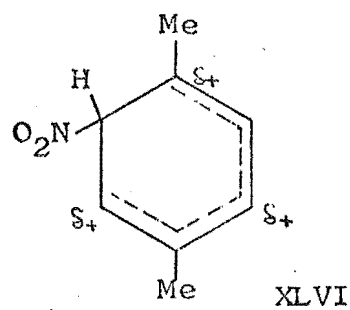
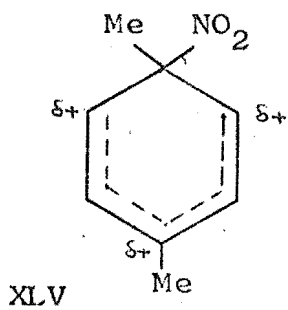
	<u>Ring position</u>				<u>Reference</u>
	C ₁	C ₂	C ₃	C ₄	
toluene	0.972	1.015	0.994	1.012	101
ethylbenzene	0.971	1.017	0.994	1.012	101
fluorobenzene	1.007	1.042	0.984	1.021	101
anisole	0.983	1.063	0.979	1.038	101
chlorobenzene	+0.014	-0.001	+0.010	-0.005	102
biphenyl (planar)	-0.006	-0.012	+0.008	-0.020	103
biphenyl (perpendicular)	+0.003	-0.013	+0.013	-0.033	103

The stabilities of transition states also are dependent on electronic and steric factors.

Both the ground state and transition state approaches explain, qualitatively at least, the observed product distributions arising from the nitrations of para-diethylbenzene and para-ethyltoluene compared to the previously nitrated para-xylene^{11,14}. The transition state approach best explains the product distributions obtained from nitration of the various mono-substituted mesitylenes.

Product distributions from para-diethylbenzene and para-ethyltoluene

In ground state terms, the quantum mechanical calculations show that only small differences are created in π -electron densities around a benzene ring by changing the ring substituent from a methyl group to an ethyl group (Table XXII). Therefore, the relative electronic activation of the substituted and unsubstituted positions in para-diethylbenzene and para-xylene are expected to be similar. The transition state approach leads to the same conclusion. The transition states for nitronium ion attack at the substituted and unsubstituted positions of para-xylene and para-diethylbenzene are discussed in terms of the ions (XLV - XLVIII) which result from attack at these positions. The transition state leading to the most stable ion is expected to be the one most favoured. In this case, as all the ions (XLV - XLVIII) carry some



positive charge on one ring position substituted by either an ethyl or methyl group and the remaining positive charge on two unsubstituted ring positions, they are expected to be of similar electronic stability. In terms of steric considerations, the ground state and transition state approaches also lead to similar conclusions. The ethyl group hinders attack at the ortho position compared to the methyl group primarily because of its greater size as has been shown many times in the study of ortho:para product ratios obtained from nitration of toluene and ethylbenzene.¹⁰⁴⁻¹⁰⁷ The ethyl group may also hinder attack at the ipso position more than a methyl group again because of its greater size. However, provided the methyl and ethyl groups offer the same comparative amounts of steric inhibition towards attack at the ipso and ortho positions, the difference in size between these groups is expected to have no effect on the relative amounts of ipso and normal nitration products obtained. If this is so, nitration of para-xylene and para-diethylbenzene should lead to similar ipso:non-ipso product ratios in each case. Consideration of the steric stabilities of the ions (XLV - XLVIII) leads to the same conclusion. The Et - NO₂ non-bonded interactions present in ions (XLVII and XLVIII) may be greater than the Me - NO₂ interactions of ions (XLV and XLVI), but the important factor in determining the ratio of ipso:non-ipso nitration products obtained from para-xylene and para-diethylbenzene is the comparative steric stability of

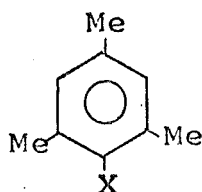
(XLV, XLVI) and (XLVII, XLVIII) respectively. Provided that (XLV, XLVI) and (XLVII, XLVIII) are of similar comparative steric stability, the nitrations of para-xylene and para-diethylbenzene are expected to give corresponding ipso:non-ipso product ratios. This condition is apparently satisfied as para-xylene (61:39)¹⁴ and para-diethylbenzene (65:35) are found to undergo ipso and non-ipso nitration to much the same extent.

If it is assumed that the methyl and ethyl substituted positions of para-ethyltoluene are equally electronically activated towards electrophilic attack, the para-ethyltoluene nitration product distribution provides a comparison between the steric hindrance the methyl and ethyl groups offer toward ipso-nitration. Furthermore, the ratio of 2-nitro-4-ethyltoluene to 3-nitro-4-ethyltoluene will be primarily a comparison of the steric hindrance offered toward nitronium ion attack ortho to a methyl group and an ethyl group respectively. The results show (Table XXI, page 82) that of the nitration products obtained from para-ethyltoluene, 38% arise from ipso-nitration at the methyl substituted position and 30% from the ethyl substituted position. 2-Nitro-4-ethyltoluene accounts for 18% and 3-nitro-4-ethyltoluene for 14% of the products. As expected, this suggests that the positions ipso and ortho to an ethyl group are slightly more hindered toward nitronium ion attack than the sites ipso and ortho to a methyl group. Furthermore, the ratio of products arising from nitration ortho and ipso to the methyl group, 18:38,

is similar to that for the ethyl group, 14:30 again supporting the assumption that the same relative steric hindrance is offered towards nitro attack at the positions ipso and ortho to a methyl or ethyl group.

Product distributions from the monosubstituted mesitylenes

Using the same approach to rationalise the nitration product distribution of the mesitylene series (XLIX,



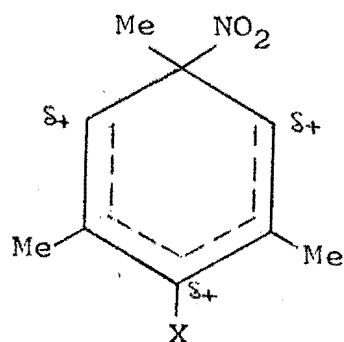
XLIX

X = Br, Cl, F, OMe, Et, C₆H₅) is more involved because there are now four different positions at which nitronium ion attack may occur. These are the positions ipso, ortho, meta and para to the substituent X.

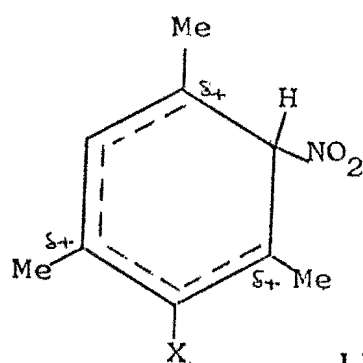
Attack at the sites ortho and para to the X-substituted position are ipso-nitrations but in the following discussion this term is reserved for nitration at the X-substituted position. Attack at the positions ortho and para to the X-substituent are termed ortho and para attack respectively.

For these molecules it is not possible to predict the most activated ground state ring position with any certainty. The results may be explained by consideration of the stabilities of the transition states, discussed in terms of the ions (L-LIII), arising from nitronium ion attack at the various ring positions.

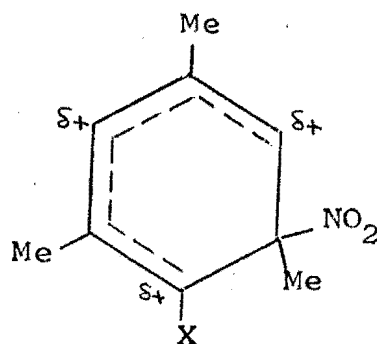
Ions resulting from ipso, ortho, meta and para nitro
attack on the X-substituted mesitylenes



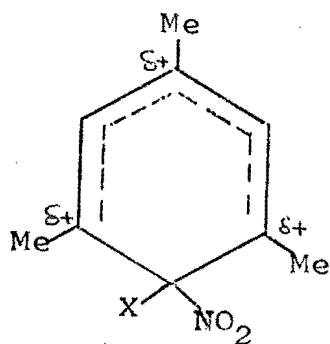
L



LI



LII

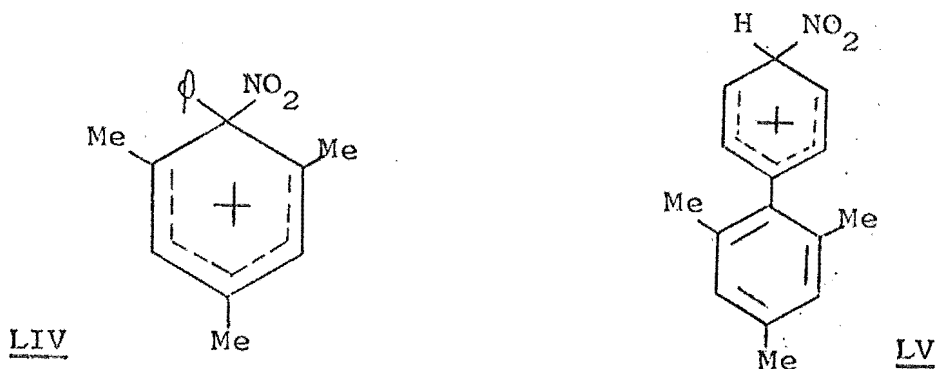


LIII

Any electrophilic attack ortho or para to the X-substituted position places a formal positive charge at the unsubstituted positions (L,LII) whereas meta and ipso-nitration result respectively in the more stable ions (LI,LIII) in which the formal positive charge resides on methyl-substituted ring positions. (L) can only be stabilised if the X-substituent is able to remove some positive charge from the ring. Of the substituents studied in this work, the methoxy group has the greatest capacity for dispersal of positive charge and, in the case of methoxymesitylene, para-nitration (via L) is now sufficiently favoured to compete with ipso-nitration (via LIII). In the other cases, the X-substituents spread positive charge less efficiently and ipso and meta-nitration become favourable; chloro, ethyl and bromo-mesitylene undergo nitration ipso and meta to the chloro, ethyl and bromo groups respectively. While this broadly explains some of the observed product distributions obtained from nitration of the substituted mesitylenes, some of the results require a closer examination.

Phenylmesitylene and other biphenyl compounds

The lack of ipso-nitration at the phenyl-substituted ring position of phenylmesitylene can be rationalised by comparison of the steric and electronic stability of the transition state (discussed in terms of LIV)



resulting from nitration ipso to the phenyl group with the corresponding properties of the transition state (LV) arising from nitration at an unsubstituted ring position. LIV is sterically unstable compared to LV because of the interactions between the nitro group and the ortho hydrogen atoms on the unsubstituted ring. These interactions are not present in LV and accordingly both products isolated from the nitration of phenylmesitylene possess a 4'-nitro substituent. Electronically, (LV) is expected to be more stable than (LIV) because it retains the possibility of spreading positive charge through the inter-ring bond to the mesitylene ring, whereas the tetrahedral centre in (LIV) stops any inter-ring resonance. However, this may not be a very important factor in phenylmesitylene because the amount of double bond character between the rings is greatest when they are co-planar as this allows for maximum overlap of p-orbitals across the inter-ring bond. In phenylmesitylene the rings are expected to be twisted far from co-planarity in order to relieve steric interactions between the ortho protons and the

ortho methyl groups on the mesitylene ring. Even the steric interactions created by the introduction of a single fluoro-substituent into one of the four ortho positions of biphenyl are sufficient to twist the rings about 50° from co-planarity^{108,109} and reduce the inter-ring resonance energy to half the amount present in biphenyl itself¹¹⁰. A large amount of nitration occurs at the 3-position of the mesitylene ring suggesting that the advantage offered by inter-ring resonance in spreading positive charge is not very great because charge placed on the ring by attack at the 3-position cannot be spread in this way.

In the case of the hexamethoxybiphenyl, steric interactions in the transition state arising from nitration ipso to the phenyl group will be greater than those present in the corresponding transition state of phenylmesitylene. Whereas the steric strain in the phenylmesitylene transition state arises from interactions between the nitro group and two protons, in the case of the hexamethoxybiphenyl transition state the nitro group interacts with two methoxy groups.

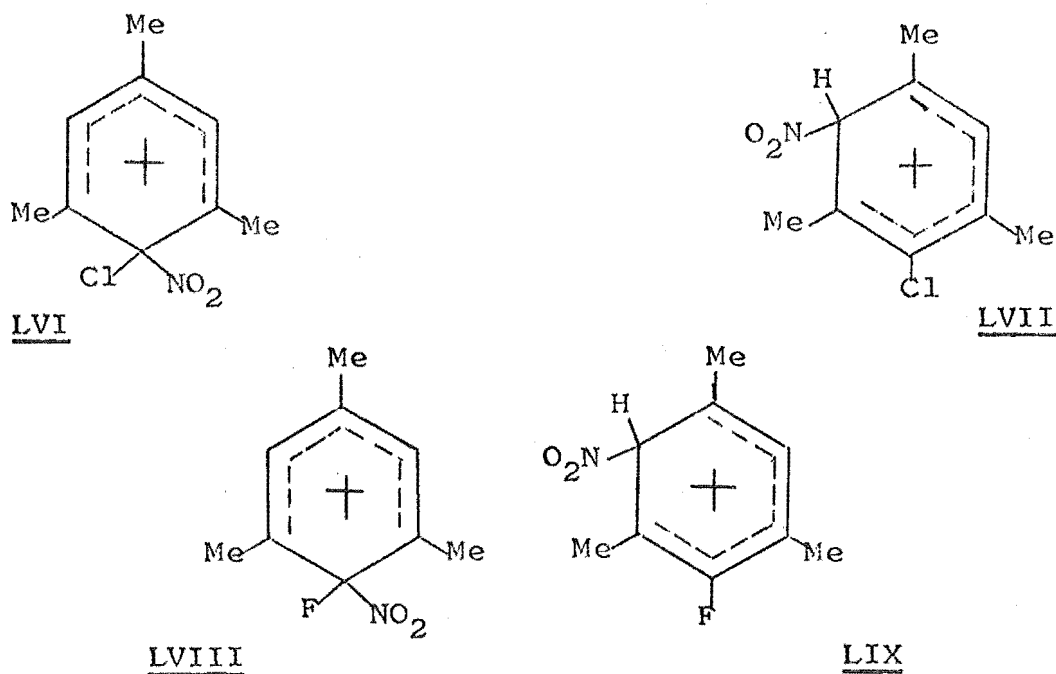
The monosubstituted biphenyls (p-bromo and p-methoxy) do not undergo nitration at the phenyl-substituted position either, again because of the steric interactions between the nitro group and the phenyl ring. Electronically, the attack at the phenyl-substituted ring position is expected to lead to the

loss of a considerable amount of inter-ring resonance. The ground state biphenyl molecule is calculated to have about 21 kJ/mole resonance energy over that of two isolated benzene rings¹¹¹. The change in inter-ring resonance energy caused by the introduction of a 4-substituent into an otherwise unsubstituted biphenyl system is small. Whatever change occurs is believed to be due to electronic interactions between the substituent and the biphenyl chromophore¹⁰⁸. Consequently, bromo and methoxy-biphenyl are not expected to undergo ipso-nitration at the phenyl-substituted position because this results in the loss of a considerable amount of resonance stabilisation energy. In fact, 4-bromobiphenyl does undergo nitration mainly at the 4'-position from where the resulting positive charge may be spread by inter-ring resonance. Other factors must be involved however, because 4-methoxybiphenyl undergoes nitration mainly ortho to the methoxy group; a position from which resulting positive charge cannot be distributed by inter-ring resonance.

The halomesitylenes

Bromo and chloro-mesitylene undergo nitronium ion attack at the sites ipso and meta to the bromo and chloro-substituted positions whereas fluoromesitylene undergoes attack only meta to the fluorine atom. This trend may be rationalised in terms of electronic and

steric stability of the relevant transition states although it is not possible to ascertain the relative importance of each effect. The results suggest (p.46)



that the transition states leading to (LVI and LVII) are of a comparable stability as both ipso and meta attack are observed in the nitration of chloromesitylene. However, (LVIII) is unstable relative to (LIX) judging by the product distributions because only meta-nitration is observed for fluoromesitylene. The relative electronic stabilities of the ions (LVI, LVII) and (LVIII, LIX) are expected to be similar because in all cases the positive charge acquired in the ring is concentrated at the methyl-substituted ring carbons. The substituent (F or Cl), located one bond away will have a minor resonance electronic effect as it is unable to

stabilise any of the ions by the spreading of positive charge. Inductively, however, the fluorine atom is able to polarise a C-F bond more than the chlorine atom polarises a C-Cl bond¹¹² and, consequently, the ring carbon ipso to the fluorine atom of fluoromesitylene may carry a greater positive charge than the corresponding carbon in chloromesitylene. Therefore, it is expected that less ipso-nitration will occur at the halo-substituted position of fluoromesitylene due to greater electrostatic repulsion between the approaching nitronium ion and the slightly positively charged ipso reaction site.

Ion (LVII) possesses a chloro-substituent and two adjacent methyl groups all of which lie in one plane, whereas ion (LVI) has a non-coplanar chlorine atom. The amount of strain associated with the three adjacent substituents in (LVII) is difficult to assess although calculations of the heats of reaction for the isomerisation of iso-propylbenzene to hemimellitene and mesitylene in the liquid state at 25° (Table XXIII) indicate there is an extra 5.04 kJ/mole required to form hemimellitene. This is due, presumably, primarily to the steric interactions between the three adjacent methyl groups in hemimellitene. The strain in (LVII) will be less than 5.04 kJ/mole judging by the relative van der Waal radii (Table XXIV) and the steric substituent constants (Table XXV) for a chlorine atom and a methyl group.

Table XXIII¹¹³

	<u>ΔH isom. (kJ/mole)</u>
Hemimellitene	-20.2 ± 0.9
Mesitylene	-25.2 ± 0.9

Table XXIV¹¹⁴

Van der Waal radii of some nonmetallic atoms (Angstroms)

F	1.35
Cl	1.80
Br	1.95
Me	2.0

Table XXV¹¹⁵

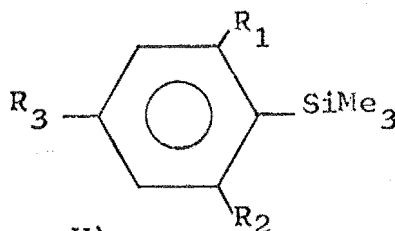
Steric substituent constants relative to F

F	0.00
Cl	-0.31
Br	-0.49
Me	-0.49

The relative steric substituent constants and van der Waal radii for F and Cl suggest there is greater strain present in (LVII) than (LIX). Consequently, it is expected that the drive to reduce steric strain will be greater in the case of chloromesitylene. Provided the transition state is not so far advanced as to lead to prohibitive steric interactions between the entering nitro group and the chlorine atom, this

strain may be relieved to some extent by the formation of a tetrahedral centre at the chloro-substituted ring position (LVI) which pushes the chlorine atom out of the plane of the adjacent methyl groups. Attack of nitronium ion meta to the chloro-substituent leads to (LVII) in which none of the strain is relieved. Judging by the van der Waal radii and steric substituent constants (E_s) for bromo and ethyl groups, the drive to relieve steric strain will be greater for bromo and ethyl-mesitylene than chloromesitylene - E_s for the ethyl group is -0.07 relative to the methyl group 0.00. This is in accord with the observed order of ipso-nitration at the non-methyl substituted mesitylene ring positions; $Et > Cl > F$.

A similar explanation has previously been used to explain the rapid rate at which (LXI) is observed



(LX) $(R_1 = R_2 = R_3 = H)$

(LXI) $(R_1 = R_2 = Me, R_3 = H)$

(LXII) $(R_1 = R_3 = Me, R_2 = H)$

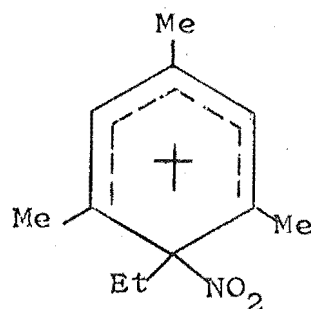
to undergo protodesilylation. (LXI) is expected to react 335 times faster than (LX) but it is found to protodesilylate 3,530 times more quickly¹¹⁶. The slow step in protodesilylation involves the formation

of a tetrahedral centre at the SiMe_3 substituted ring position pushing the SiMe_3 group out of the plane of the two neighbouring methyl groups (in the case of LXI) and relieving the steric strain present in the reactant molecule. In the case of (LXII), less steric strain stands to be relieved and in accordance with this, (LXII) reacts only 417 times faster than (LX), close to the calculated rate.¹¹⁶

In this work however, any steric acceleration will be considerably less than that observed in the proto-desilylation studies: (i) because the leaving group, SiMe_3 , is larger than Cl, Br or Et and (ii) because the attacking species, H^+ is smaller than NO_2^+ .

As mentioned previously, it may be misleading to compare the product distributions obtained from reactions involving ipso-nitration at ring positions bearing substituents of different leaving ability. Therefore, the failure to observe any ipso-nitration at the fluoro-substituted position of fluoromesitylene may be due to loss of NO_2^+ from (LVIII) before subsequent reactions leading to recognisable ipso-products can occur.

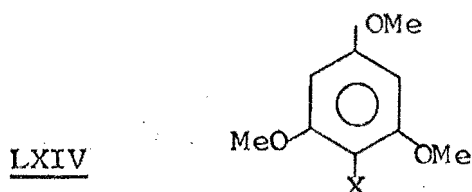
However, on the basis of the relative leaving abilities of Cl^+ and Et^{+12} , it seems probable that NO_2^+ will leave



LXIII

(LXIII) more readily than (LVI) and therefore, if reversibility of ipso attack were an important factor, it is expected that the chloro-substituted position of chloromesitylene would exhibit at least as much ipso-nitration as the ethyl-substituted position of ethylmesitylene. The results show that this is not so.

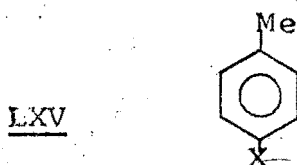
The analogous series of methoxy compounds (LXIV,



X = Br, Cl, F) show the same trends as the mesitylene series. The fluoro derivative gives no products arising from ipso-nitration at the fluorine-substituted position; the chloro derivative gives 25% (chloromesitylene 20%) and the bromo derivative a significant, but incalculable amount of ipso-nitration products. Similar reasoning may be used to rationalise these results.

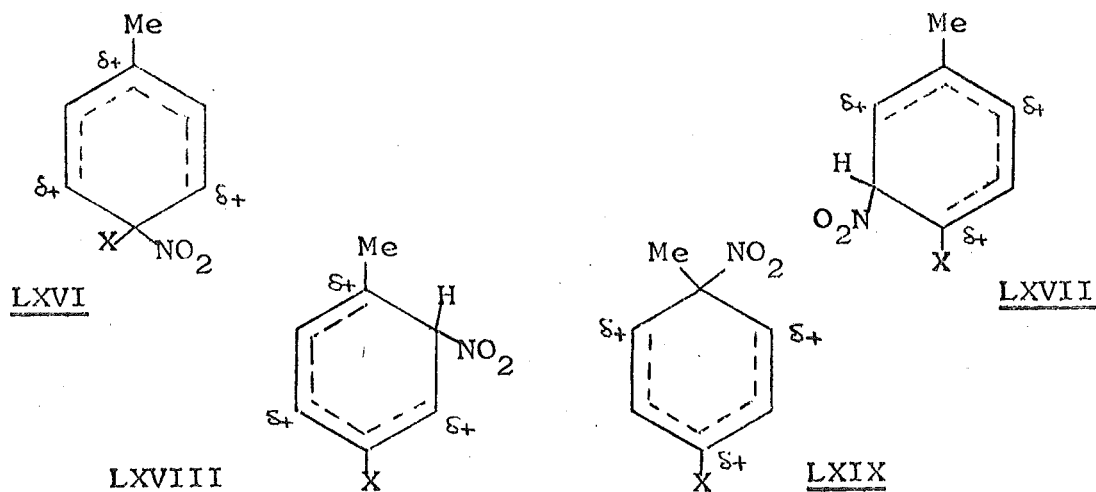
Other nitrations

Other compounds nitrated in this work exhibit varying degrees of ipso-nitration at methyl-substituted ring positions. The toluenes (LXV, X = OMe, Br, OAc)



undergo nitration ipso to the methyl group as well as substantial amounts of nitration at the unsubstituted

ring positions. The transition states arising from attack ipso, ortho, meta and para to the X-substituent lead to the ions (LXVI - LXIX) all of which have some positive charge located either at the methyl or X-substituted position. The relative electronic stability



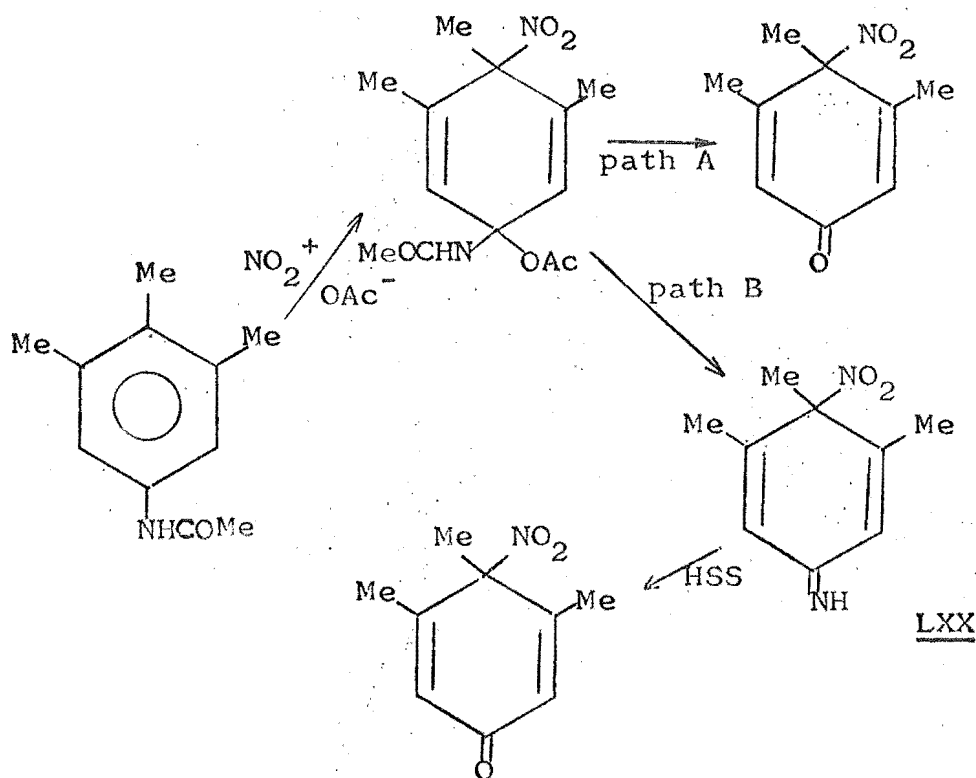
of these ions will, therefore, depend to a large extent on the ability of the X group to enter into resonance with the ring and disperse positive charge. The methoxy group is well able to spread charge in this way and those ions (LXVII, LXIX) which place positive charge on the X-substituted ring position will be favoured most in the case of para-methoxytoluene. Accordingly, the only products obtained from the nitration of para-methoxytoluene in nitric acid-acetic anhydride arise from nitronium ion attack at the ring positions ortho and para to the methoxy group.

Para-acetoxytoluene undergoes nitration ortho, meta and para to the acetoxy derivative. Ipso-nitration is not observed presumably because the acetoxy function is

sufficiently bulky to render such attack unfavourable.

Not all the products of para-bromotoluene nitration were isolated and identified. Nitration certainly occurs ortho and para to the bromo substituent. No compounds arising from ipso or meta nitration were isolated although the possible formation of a dibromo compound suggests nitration ipso to the bromine atom by analogy with bromomesitylene (page 93).

Nitration of 3,4,5-trimethylacetanilide gives 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one as the major product. This may arise either by the normal pathway (A) or via path (B) involving the formation of an imine (LXX) and its subsequent rapid hydrolysis.

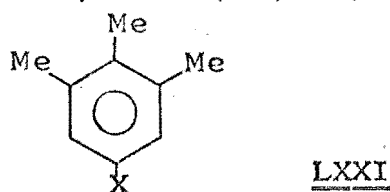


Scheme (XXVI)

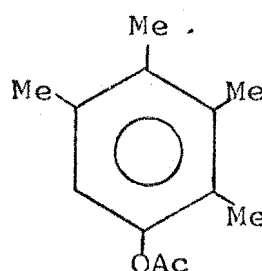
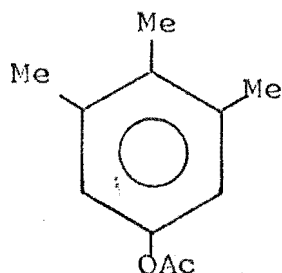
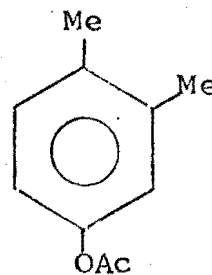
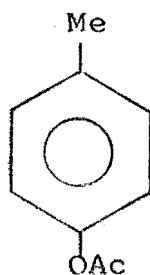
Such imines undergo hydrolysis very easily with water and are seldom sufficiently stable to be isolated¹¹⁷. Although Ac_2NH is released during reaction via path (A), this does not help distinguish it from path (B) because this side product will probably escape detection. Under the reaction conditions used, Ac_2NH is likely to be converted to acetic acid by protonation and hydrolysis.

Competition nitrations

The aim of this section is (i) to study the effect on the rate of ipso-nitration at the central methyl group in the series (LXXI, $\text{X} = \text{F}, \text{H}, \text{Br}, \text{OAc}, \text{OMe}, \text{NHAc}$)



and (ii) to study the effect on the rate of ipso-nitration at the methyl group para to the acetate function in the series (LXXII)



The nitration reactions are all very rapid and measurement of the rates of each individual reaction may not be of sufficient accuracy to show up the rate differences. For this reason the reactions were run as competitions between pairs of compounds and in this way rate differences showed up markedly. As ipso-nitration occurs at ring positions bearing the same substituent (methyl group) throughout the two series, any difficulties associated with the possible reversibility of ipso-nitration are likely to be minor.

The first step in the nitration reaction is either ipso-nitration or normal nitration of the aromatic compound. Therefore, the relative rate of disappearance of the two compounds in any particular competition reaction reflects the rate at which these compounds undergo nitration (ipso and normal) relative to each other. Provided it is possible to determine the extent to which each compound undergoes ipso-nitration, the relative rate of disappearance will allow a measure of the relative rate of ipso-nitration. Analysis of the product mixtures obtained from the competition nitrations between acetoxyhemimellitene and bromohemimellitene (p.55) and acetoxyhemimellitene and hemimellitene (p.56) show in both cases that these compounds are each reacting to give the same proportion of ipso product (dienone) in competition as given when nitrated in isolation. The same is assumed to apply in the other cases. Thus, all the 5-substituted hemimellitenes, except methoxy, undergo

nearly the same amount (65%) of ipso-nitration. (Table XXVI)

Table XXVI

<u>5-X-hemimellitene</u>	<u>% ipso-product</u>
X = F	67
OAc	72
Br	65
NHAc	55
OMe	31
H	33

A competition nitration reaction between two substrates competing for the same reagent (NO_2^+) gives meaningful results only if the reaction is first order in substrate and if the reaction of NO_2^+ with one of the reactants does not affect the reaction of NO_2^+ with the other reactant. Provided these conditions are met, the ratio (r) of specific rate constants can be calculated from the equation:-^{118,119}

$$r = \frac{\log \text{ of fraction of reactant A remaining}}{\log \text{ of fraction of reactant B remaining}}$$

It is important that the ratio of concentrations of both reactants is uniform throughout the reaction mixture. This is helped by vigorous stirring of the reaction mixture and can be tested by making determinations of r in which the initial ratios of concentration of reactants are varied. If r remains constant, the mixing is adequate. This was found to be the case, for when hemimellitene and

acetoxyhemimellitene (2:1 molar ratio) undergo competitive nitration, the ratio of rate constants stays at 18:1.

The figures calculated for r are not as important or as accurate as the trends they show. When the ratio of rate constants is greater than ten it becomes difficult to gain an accurate figure for r because a great deal of the more reactive competition species disappears before any significant change is noticed in the concentration of the less reactive competitor. When r is greater than 30 it is not possible to detect any accurate change in concentration of the less reactive species before essentially all the reactive compound disappears. Consequently, attempts to plot the competition reaction between, for example para-acetoxytoluene and 4-acetoxy-o-xylene lead to unsatisfactory graphs and the only conclusion in such a circumstance is that 4-acetoxy-o-xylene is reacting over thirty times faster than para-acetoxytoluene.

The relative rates of nitration obtained from the hemimellitene series should allow an estimate of the ρ value for ipso-nitration to be made. Since

$$\log k_x = \rho \sigma_x^+ + \text{constant}$$

$$\log k_H = \rho \sigma_H^+ + \text{constant}$$

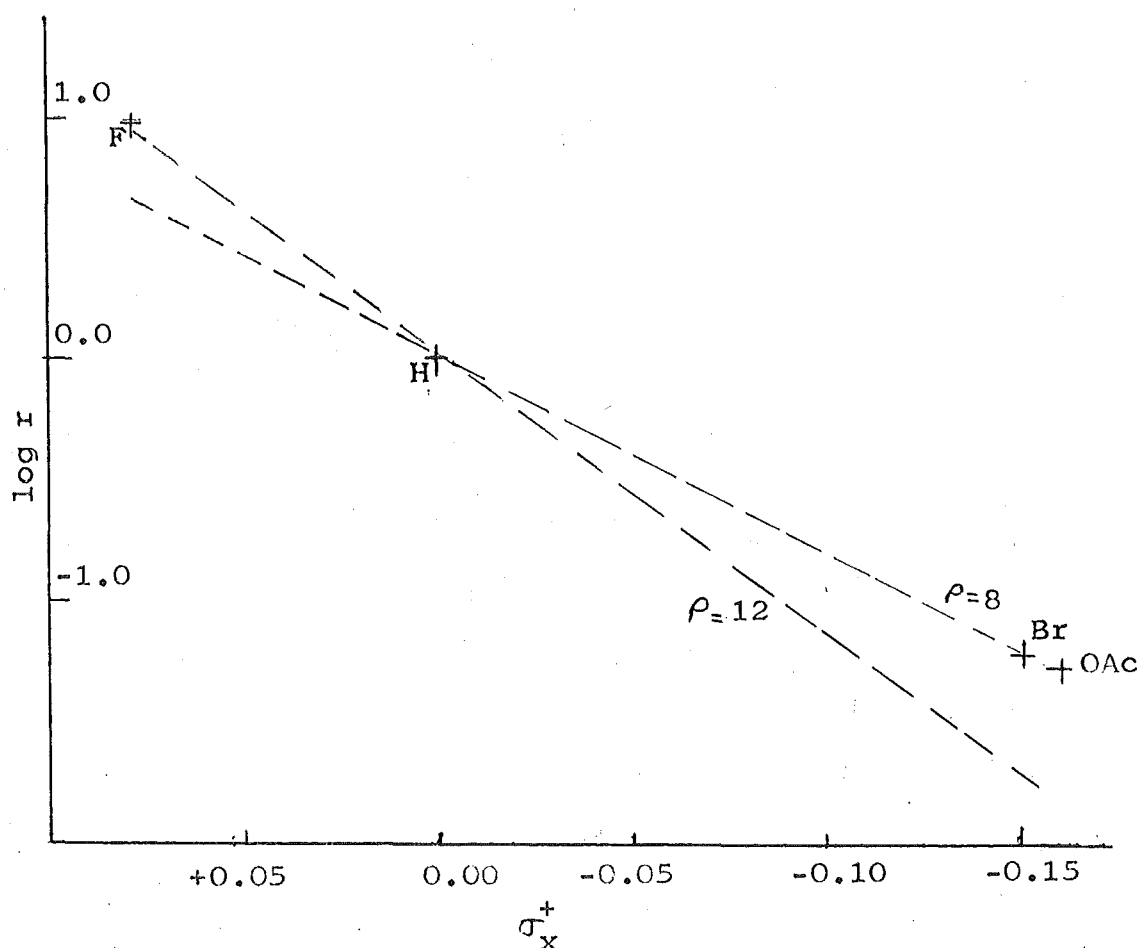
$$\log \frac{k_x}{k_H} = \rho (\sigma_x^+ - \sigma_H^+) + \text{constant. As } r = \frac{k_x}{k_H}$$

$$\log r = \rho (\sigma_x^+ - \sigma_H^+) + \text{constant. } \sigma_H^+ = 0$$

$$\log r = \rho \sigma_x^+ + \text{constant.}$$

A plot of $\log r$ v σ_x^+ will therefore be a straight line

of slope ρ . Unfortunately, the r value was obtained only from the bromo ($\sigma_{\text{P-Br}}^+ = +0.15$), acetoxy ($\sigma_{\text{P-OAc}}^+ = +0.16$) and fluoro ($\sigma_{\text{P-F}}^+ = -0.07$) hemimellitenes relative to hemimellitene ($\sigma_{\text{H}}^+ = 0.00$) and consequently, such a graph is not very reliable because there are effectively only three points on it. 5-Methoxyhemimellitene ($\sigma_{\text{P-OMe}}^+ = -0.78$) and 3,4,5-trimethylacetanilide ($\sigma_{\text{P-NHAc}}^+ = -0.75$)¹²⁰ react so much more rapidly than hemimellitene that a value of r was unobtainable by the competition technique. Therefore, while it is certain that the rate of ipso-nitration at the 2-substituted position of hemimellitene is very sensitive towards substituent changes in the 5-position, the exact ρ value for the reaction is not known although the graph below suggests this value lies between 8 and 12.



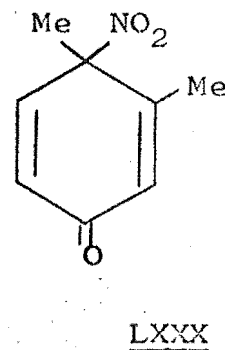
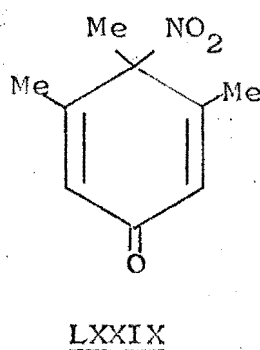
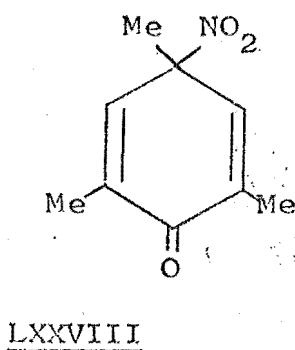
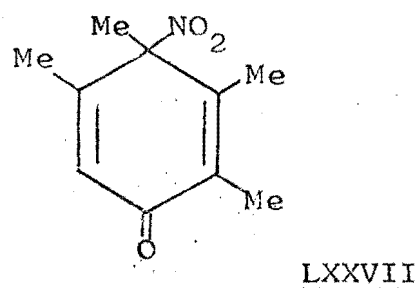
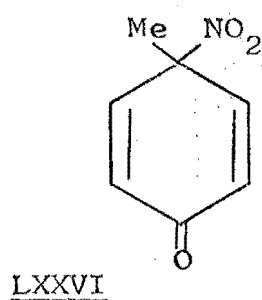
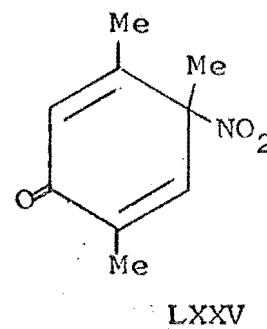
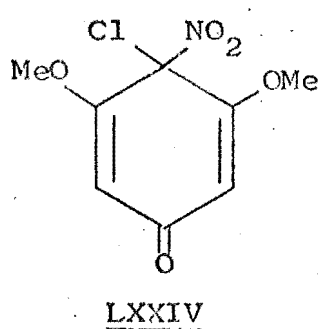
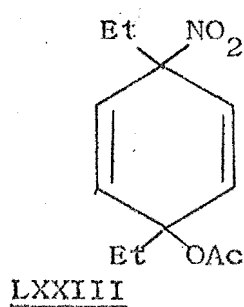
The addition of an extra methyl group ortho to the site of ipso-nitration in the series (LXXII, p.114) increases the rate of ipso-nitration sufficiently to make an accurate measurement of r impossible. Thus 4-acetoxy-o-xylene reacts much more rapidly ($r > 30$) than para-acetytoluene and 5-acetoxymellitene reacts much more rapidly ($r > 30$) than 4-acetoxy-o-xylene. These results are consistent with the fact that the extra methyl group ortho to the site of ipso-nitration in both cases strongly activates this position towards electrophilic attack. This is reflected by a large rate increase in this substituent-sensitive reaction. Acetoxymellitene reacts 7 times faster than 5-acetoxymellitene, consistent with a value of 12 ($\sigma_m^+ = -0.07$).

The most important point to emerge from the work in this section is that, provided ipso-nitration occurs via a transition state of comparable stability to that of a "normal" nitration, it may be expected that both ipso-nitration and normal ring nitration products will be formed. It is expected, therefore, that ipso products will be formed from the nitration of many aromatic compounds in nitric acid-acetic anhydride. The fact that "anomalous" nitration products in this medium have, in the main, been discovered only recently may be due to workers using the method simply as a means of preparing nitro-substituted aromatic compounds and using isolation

techniques that leave the other nitration products such as side-chain nitro compounds and aryl acetates undetected. It is noticeable in some cases that quite low yields of nitro compounds have been obtained¹²¹, suggesting that some ipso products may have been formed but not isolated.

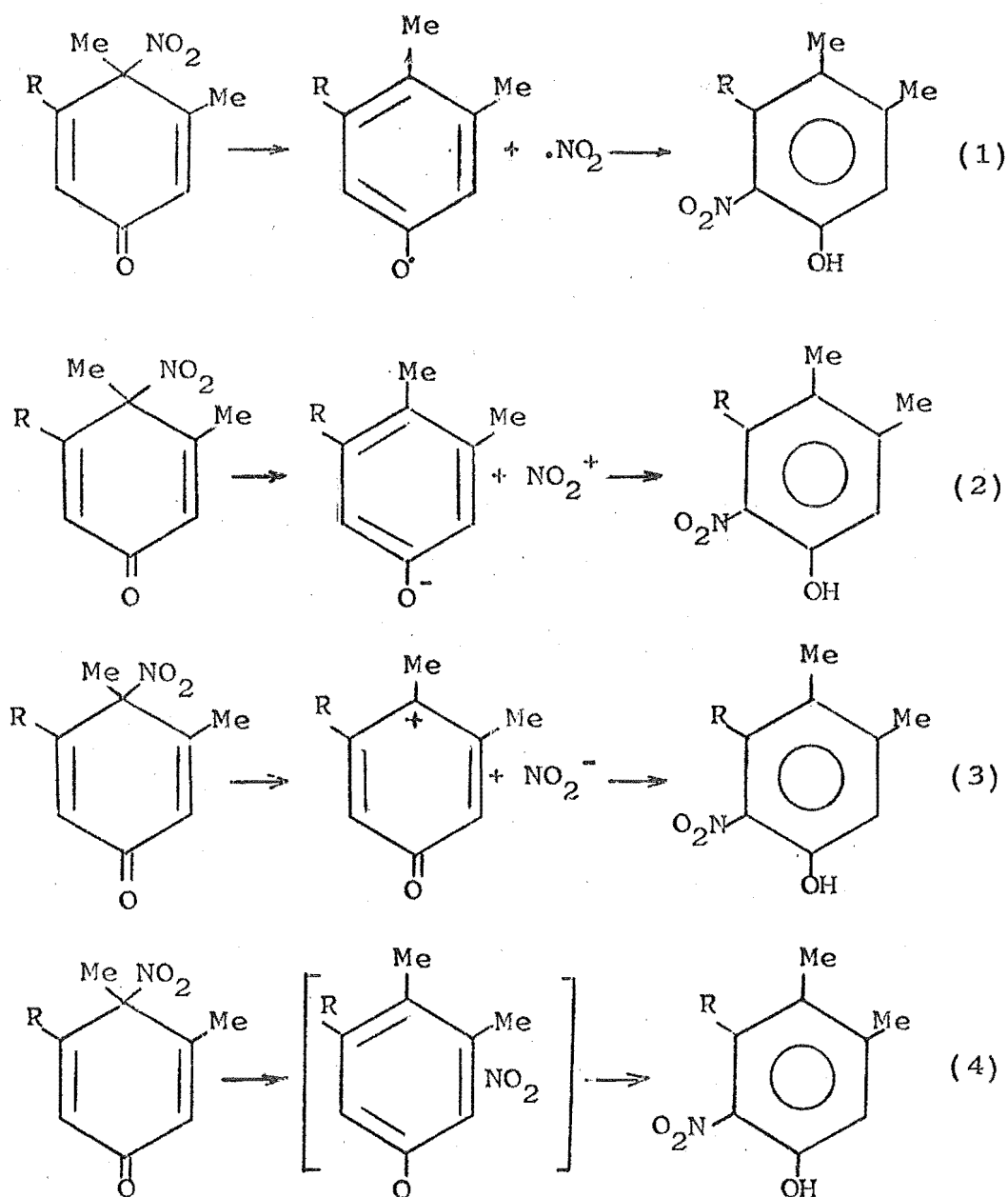
Rearomatisation of diene and dienone intermediates

The dienone intermediates isolated in this thesis (LXXIV - LXXX) rearomatise to give nitrophenols. The



isomer of diene (LXXIII) isolated from the nitration of para-diethylbenzene undergoes rearomatisation in aqueous acetic acid to give acetoxy-p-diethylbenzene in an analogous way to the diene adducts isolated from para-xylene.⁹⁵ Dienone (LXXVIII), isolated from the nitration of methoxymesitylene, is stable for several months at 0° and decomposes at 150° by loss of the nitro group to give mesitol presumably because the positions most favoured towards nitro attack (ortho and para to the oxy function) are blocked. In all other cases there is at least one unsubstituted ring position ortho to the oxy function and ortho-nitro-phenols are the favoured rearomatisation products. Dienones (LXXIX, LXXX) rearrange cleanly under most conditions and an investigation of the rearomatisation mechanism was carried out in this thesis.

Four rearomatisation mechanisms have previously been presented¹²² (scheme XXVII). In reaction(4), which is totally intramolecular, the nitro group either migrates around the ring or is trapped in a solvent cage and reattacks the ring before it is able to "escape" from this cage. Reactions (1) - (3) are intermolecular and the nitro group is free to react with introduced species provided they are of sufficient reactivity. Therefore, addition of an external source of N^{15} ($NaN^{15}O_2$) to the rearranging dienone system will enable a distinction to be made between the intra- and intermolecular rearomatisation mechanisms. If the



R = H, Me

Scheme (XXVII)

rearrangement is totally intramolecular, none of the external N^{15} will be incorporated into the product(s) (nitrophenol(s)) whereas an intermolecular reaction is expected to lead to N^{15} incorporation among the products as a result of nitrogen scrambling between the free nitro group and the $N^{15}O_2^-$ or possibly by direct

reaction between $\text{N}^{15}\text{O}_2^-$ and the ring.

The rearrangements were carried out in methanol. This was chosen as the most suitable solvent¹²³ on the basis of the following criteria. Firstly, the solvent must be able to dissolve both the dienone and N^{15} sodium nitrite; secondly, the rearrangement must go cleanly; thirdly, the solvent must be inert and fourthly, the reaction time for >95% rearomatisation should be neither too short (<four hours) nor too long (>two to three weeks).

The results show (Table XII, XV p.58 and 60) that both dienones rearrange to nitrophenols with accompanying N^{15} incorporation ruling out the totally intramolecular rearomatisation mechanism (4). As most rearrangements are performed using a 1:1 molar ratio of dienone: N^{15} nitrite, there is expected to be an equal amount of N^{15} enriched and unenriched product if the reaction is totally intermolecular and provided one released N^{14} nitro group undergoes nitrogen exchange with one N^{15} nitrite ion. In that case the $\text{N}^{15}/\text{N}^{14}$ ratios in tables XII and XV will be unity but these ratios are actually 0.42 and 0.18 for the dimethyl dienone and trimethyl dienone respectively. Such N^{15} incorporation results show only that the dimethyl dienone rearrangement incorporates significantly more of the available N^{15} .

The rearrangement mechanism

The kinetic studies indicate (Tables XVIII and XIX,

p. 62) that the rearrangements are first order in dienone and insensitive to the addition of nitrite ions. Thus the slow step of the rearrangement involves only the dienone and, as the rearrangement is known to be intermolecular to some extent, probably involves the cleavage of the dienone into a nitro fragment and a corresponding ring fragment. The nitro group may be released either as a nitrite ion, free radical or nitronium ion and on the basis of the following evidence, the most likely species is the nitronium ion.

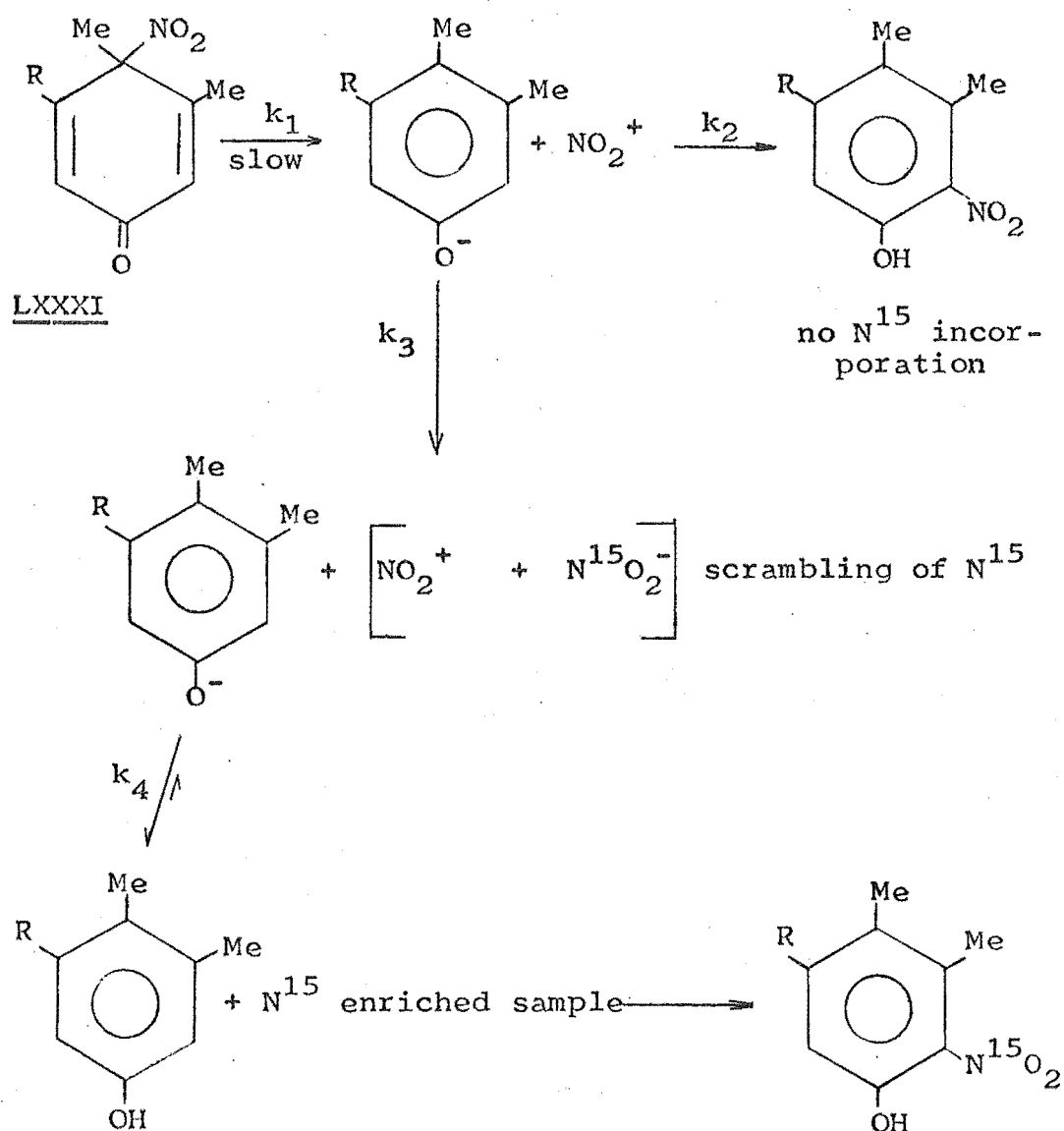
If the first step in the rearomatisation involves cleavage of the dienone into nitronium ions and the corresponding phenoxide ions then an introduced species, provided it is sufficiently activated, will trap some of the free nitronium ion to give a cross-nitration product. This prediction was tested by rearranging the dimethyl dienone in the presence of an equimolar amount of 3,4,5-trimethylphenol. This gave a mixture of nitrophenols of which 36% was the cross-nitration product, 2-nitro-3,4,5-trimethylphenol. Doubling the amount of available 3,4,5-trimethylphenol increased the cross-nitration to 45% and the addition of further quantities of the phenol did not significantly alter the proportion of cross-nitration product. Halving the concentration of 3,4,5-trimethylphenol halved the amount of cross-nitration. These results are discussed later. Cross-nitration was also observed between the dimethyl dienone

and resorcinol (1,3-dihydroxybenzene) and phloroglucinol (1,3,5-trihydroxybenzene). This evidence does not rule out the possibility that the nitro group is released from the dienone as a free radical because this species is also able to attack aromatic substrates¹²⁴ but the evidence does rule out the possibility that the dienone cleaves to release a nitrite ion as such a species is unable to nitrate 3,4,5-trimethylphenol under the rearrangement conditions. This was shown by allowing a solution of 3,4,5-trimethylphenol and sodium nitrite in methanol to stand for two weeks during which time no reaction occurred. Nitrite ion release is also ruled out by the highly sensitive Griess-Ilosvay test which is capable of detecting nitrite ion concentrations as low as 1 mg./l.¹²⁵ However, samples taken from a trimethyl dienone rearrangement at time intervals ranging from 30 seconds to 5 days after the start of the reaction all gave negative Griess-Ilosvay tests. Similarly, samples taken from a dimethyl dienone rearrangement between 30 seconds and 1 day after the start of rearomatisation contained no nitrite ion by the Griess-Ilosvay test.

The possibility of the nitro group being released as a free radical is considered unlikely because no significant rate enhancement results when the rearrangement conditions are altered to favour a free radical mechanism. Thus performing the rearrangement under ultraviolet light or in the presence of dibenzoyl

peroxide does not change the rate of rearomatisation or the rearomatisation products. Other factors not considered favourable to a free radical mechanism are the polar solvent methanol, which is more favourable to ion formation, and the low temperature at which the reactions are run. Free radical reactions are favoured by elevated temperatures.

The reaction mechanism suggested by this study is outlined in scheme XXVIII.



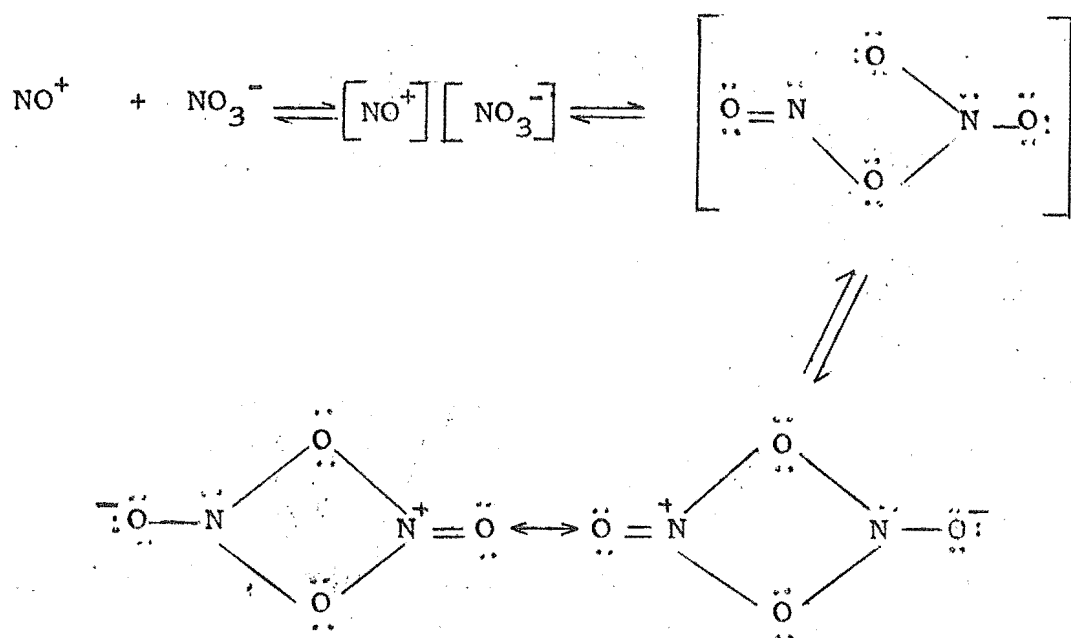
Scheme (XXVIII)

This mechanism explains the results summarised on p. 64. The fact that the trimethyl dienone (LXXXI, R = Me) rearranges more slowly, $k = 3.7 \times 10^{-6} \text{ sec}^{-1}$, than the dimethyl dienone (LXXXI, R = H) $k = 7.0 \times 10^{-5} \text{ sec}^{-1}$ can be rationalised as follows. During the slow step, the ring carbon originally bearing both the nitro and methyl groups changes from a tetrahedral "sp³" centre to a planar "sp²" centre. Therefore, as the nitronium ion is leaving, the ipso-methyl group swings into the plane of the aromatic ring encountering greater steric hindrance as it does so from the two adjacent methyl groups of the trimethyl dienone than the single adjacent methyl group of the dimethyl dienone. The magnitude of this extra steric interaction can be estimated from the calculated heats of combustion of hemimellitene and pseudocumene in the liquid state at 25° which indicate about 3.4 kJ/mole extra strain in the hemimellitene molecule.¹²⁶ This is presumably caused primarily by the greater steric requirement of the extra methyl group flanking the C₂ position of hemimellitene.

There is less N¹⁵ incorporated into the rearrangement product of the trimethyl dienone ($N^{15}/N^{14} = 0.18$) than the dimethyl dienone products ($N^{15}/N^{14} = 0.42$) primarily because the trimethyl phenoxide arising from dienone cleavage carries an extra methyl group which activates the ring more strongly towards electrophilic attack by nitronium ion; less nitronium ion will escape the trimethyl phenoxide to enable nitrogen

scrambling reactions to occur. In other words, the ratio of $k_2:k_3$ is, as expected, greater for $R = \text{Me}$ than $R = \text{H}$ (scheme XXVIII).

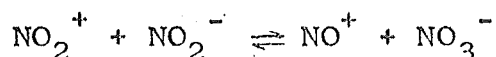
As the factor determining N^{15} incorporation is apparently the relative magnitude of k_2 and k_3 , it may be expected that doubling the amount of available N^{15} will double the N^{15} incorporation and halving the amount will lead to a corresponding decrease in N^{15} incorporation. The latter is found to be the case but doubling the N^{15} concentration only slightly increases the N^{15} incorporation suggesting that scrambling may not be a simple 1:1 reversible exchange of N^{15} between nitronium ion and $\text{N}^{15}\text{O}_2^-$. The information available concerning the reaction between nitronium and nitrite ions shows that they react rapidly and irreversibly to form NO^+ and NO_3^- by the transfer of an oxygen atom.¹²⁷⁻¹³⁰ Nitroso and nitrate ions may undergo further reaction to form N_2O_4 .



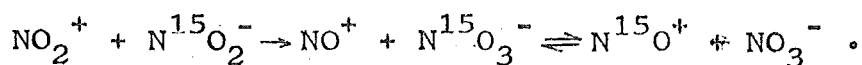
LXXXII

Scheme (XXIX)

The Longuet-Higgins structure of $N_2O_4^{131}$ then cleaves to give either two nitro radicals or to form ionic species and the polar solvent in which the reactions are run favours ion formation. These ions will necessarily be the nitroso and nitrate ions because if nitronium and nitrite ions form the overall effect will be a reversible reaction

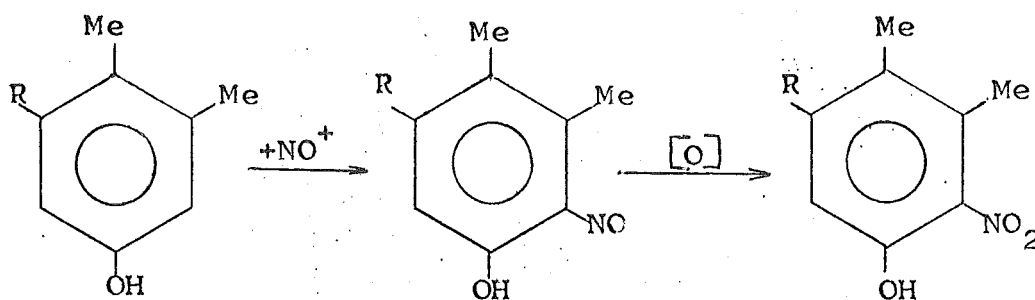


which is not in agreement with experiment.¹²⁷ Therefore, the scrambling reaction may best be represented as



Nitration of the phenol leading to N^{15} enriched products occurs, not by NO_2^+ , but by nitrosation and oxidation.

(scheme XXX)



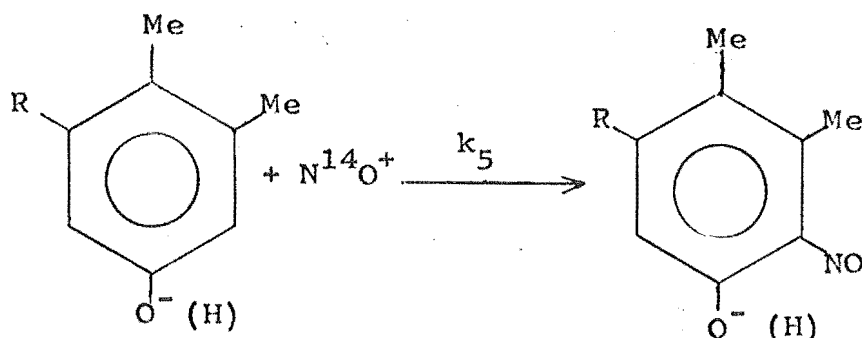
Scheme (XXX)

The requirements for C-nitrosation are (i) a nucleus that is strongly activated towards electrophilic attack and (ii) the presence of a nitrosating species.^{132,133}

The second requirement is clearly satisfied. The first condition is also met because phenols are among the few aromatic compounds sufficiently activated towards electro-

philic attack to undergo nitrosation.²⁵

This suggests that release of a nitronium ion from the phenoxide allowing scrambling with $\text{N}^{15}\text{O}_2^-$ will not lead to an N^{15} incorporation product unless the nitroso and nitrate ions undergo scrambling before the phenoxide (or phenol) reacts with the N^{14} nitroso ion. Thus the amount of N^{15} incorporation is dependent on the relative magnitudes of k_5 and k_6 (scheme XXXI) as well as k_2 and k_3 (scheme XXVIII). Neither k_5 nor k_6 (scheme XXXI)



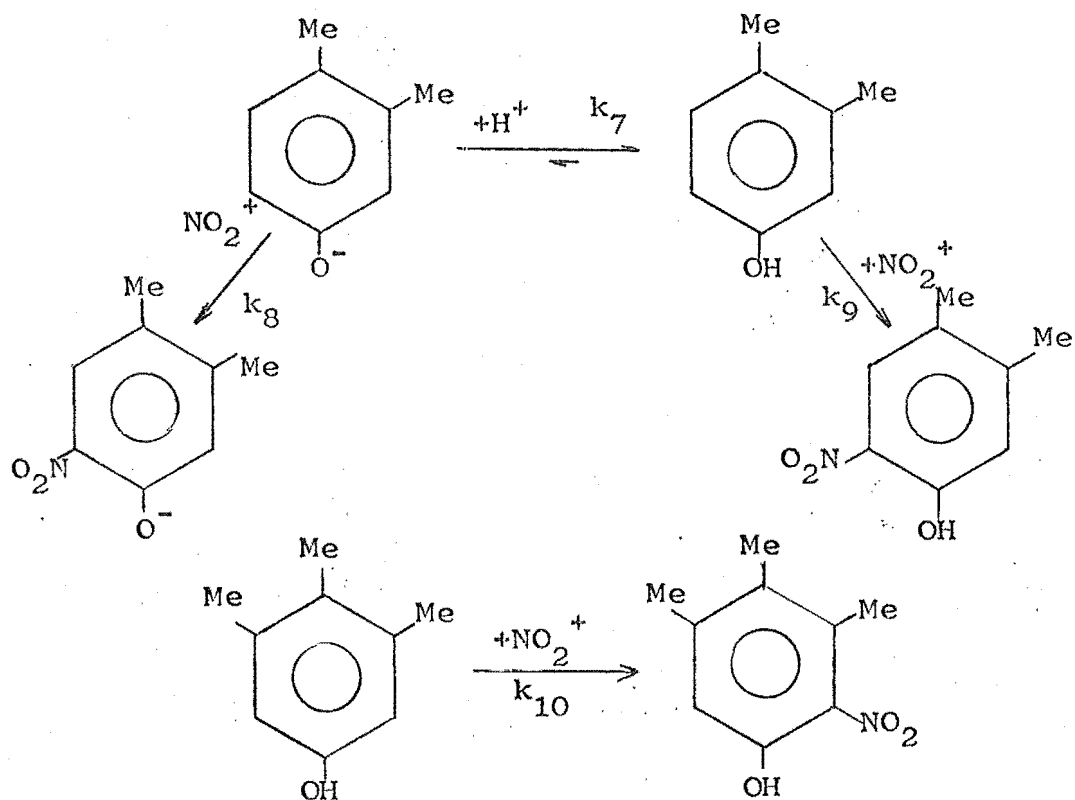
Scheme (XXXI)

is known but it should be mentioned that if $k_5 > k_6$, the N^{15} incorporation figures will be low because the above situation will then arise; i.e. some of the N^{14} nitroso ions will be trapped by phenoxide (or phenol) before they are able to undergo nitrogen exchange with the N^{15} enriched nitrate ions. This leads ultimately to iso-

topically unenriched nitrophenols via an intermolecular reaction mechanism.

The trend in N^{15} incorporation with changing N^{15} nitrite concentrations may also be explained in terms of scheme XXXI. Increasing the $N^{15}O_2^-$ concentration makes more unenriched nitroso ions available for either nitrogen scrambling or attack by phenoxide. If $k_5 > k_6$, the majority of extra nitroso ions will be removed by reaction with the phenoxide leading to little overall increase in the N^{15} incorporation. Furthermore, the N^{15} incorporation will also depend on the rate of protonation of the phenoxide. The longer the phenoxide lifetime, the greater the likelihood that it will trap nitroso ions before N^{15} scrambling can occur as phenoxides are much more activated towards electrophilic attack than the corresponding phenols.

Protonation of phenoxide is also a relevant factor in determining the extent of cross-nitration observed when the dimethyl dienone rearomatises in the presence of 3,4,5-trimethylphenol. The cross-nitration figures show a similar trend to the N^{15} incorporation results and as in the case of N^{15} incorporation, cross-nitration is dependent on the rates of several competing reactions. (scheme XXXII). The fact that cross-nitration occurs at all suggests that some of the nitronium ion is competed for by di- and trimethylphenol with the rest of the nitronium ion being trapped by dimethylphenoxide.

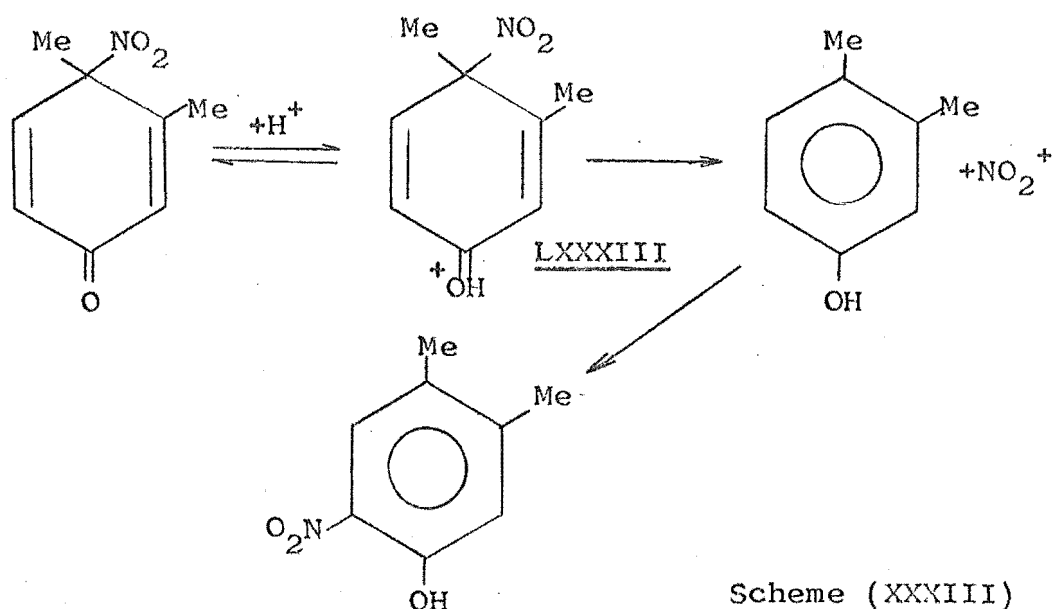


Scheme (XXXII)

As the O^- function activates the ring towards electrophilic attack much more strongly ($\sigma_{\text{P-O}^-}^+$ est. - 1.7¹³⁴) than the OH group ($\sigma_{\text{P-OH}}^+ = -0.92$), it is expected that competition for NO_2^+ between a trimethylphenol and a dimethylphenoxide will be in favour of the phenoxide and little or no cross-nitration will be observed in such a case. The observed significant amount of cross-nitration suggests either that the dienone itself is protonated before cleavage to liberate the dimethylphenol directly or that the phenoxide is protonated rapidly once formed. The first suggestion is unlikely as only a weak acid, methanol $\text{pK}_a = 16$ ¹³⁵, is available to protonate the dienone which, judging by the amounts of acid required to protonate

similar compounds, does not possess a particularly basic oxygen atom¹³⁶. In contrast, 3,4-dimethylphenoxide is a strong base, pK_a (phenol) = 10.3 in aqueous solution¹³⁷, and is able to undergo protonation with methanol or any small amounts of water that may be present in the methanol. Overall, the cross-nitration figures are very dependent on the relative magnitude of k_7 and k_8 (scheme XXXII). If $k_7 \gg k_8$, the nitronium ion is competed for by trimethylphenol and dimethylphenol and a large amount of cross-nitration is expected. If $k_7 \ll k_8$, virtually no cross-nitration is expected. The results suggest that the relative magnitude of k_7 and k_8 is somewhere between these two extremes.

As mentioned previously, compounds similar to the dienones such as cyclohexanones, require a fairly acidic medium in order to achieve half-protonation; e.g. anthrone requires 65% by weight sulphuric acid and cyclohexanone requires 79%.¹³⁶ In order to follow the dienone rearrangements by n.m.r., it was possible to have only 7-8% acid (perchloric) present otherwise the spectra became poorly resolved. Therefore, of the dienone present, the majority is unprotonated and will undergo rearrangement in the normal way by scheme XXVIII. For the small amount of protonated dienone, the nitronium ion is leaving from a positively charged species (LXXXIII, scheme XXXIII) in the slow step and the rearrangement is expected to occur more rapidly. This is seen to be



Scheme (XXXIII)

the case. Table XX (p.63) shows a comparison between two rearomatisations of dimethyl dienone; one run with 7% perchloric acid present and the other with no acid present. The important point is the immediate drop in dienone concentration in the rearrangement run in the presence of perchloric acid. This corresponds to protonation and subsequent rapid rearrangement of the dienone. Thereafter, the two reactions parallel each other closely because all the acid has been used. The acid is not regenerated after the dienone rearranges (scheme XXXIII) and the reaction cannot truly be called an acid catalysis.

It is unlikely that complications arise from side reactions. The only possibility appears to be reaction between the nitronium ion released from the dienone and methanol to form methyl nitrate.^{138,139} Although this reaction is thirty times faster than the benzene- NO_2^+ reaction¹⁴⁰, it takes twenty minutes at room temperature

in 4 mol. l^{-1} nitric acid and nitromethane to attain 50% completion¹³⁹ and is expected, therefore, to be insignificant compared to the very rapid reactions with which it is competing in this system.

The study of the rearrangements of 3,4-dimethyl-4-nitrocyclohexa-2,5-dien-1-one and 3,4,5-trimethyl-4-nitrocyclohexa-2,5-dien-1-one to their corresponding nitrophenols has established that these are intermolecular reactions involving heterolytic splitting of the dienones into phenoxide and nitronium ions. The free nitronium ion subsequently attacks a phenoxide or phenolic species at the position of highest electron density to give the nitrophenol. The details of the N^{15} scrambling mechanism are speculative to a degree but it is quite probable that the N^{15} enriched products arise by nitrosation. Certainly the NO^+ ion will be formed irreversibly as a result of reaction between NO_2^+ and $N^{15}O_2^-$ by the oxidative transfer of an oxygen atom.¹²⁷ Any change of reaction mechanism brought about by the addition of nitrite ions will go undetected because the slow step of the rearrangement remains the cleavage of the dienone and any subsequent steps have no effect on reaction rate.

The reactive species in nitric acid-acetic anhydride

Throughout this thesis the nitrating species in nitric acid-acetic anhydride has been represented as the nitronium ion, NO_2^+ , and all nitrations carried out

in this medium to date are explicable in terms of NO_2^+ as nitrating species. In fact, the nature of the nitrating species in nitric acid-acetic anhydride is not certain; protonated acetyl nitrate or nitronium ion solvated by acetic or nitric acid have also been suggested at various times.

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